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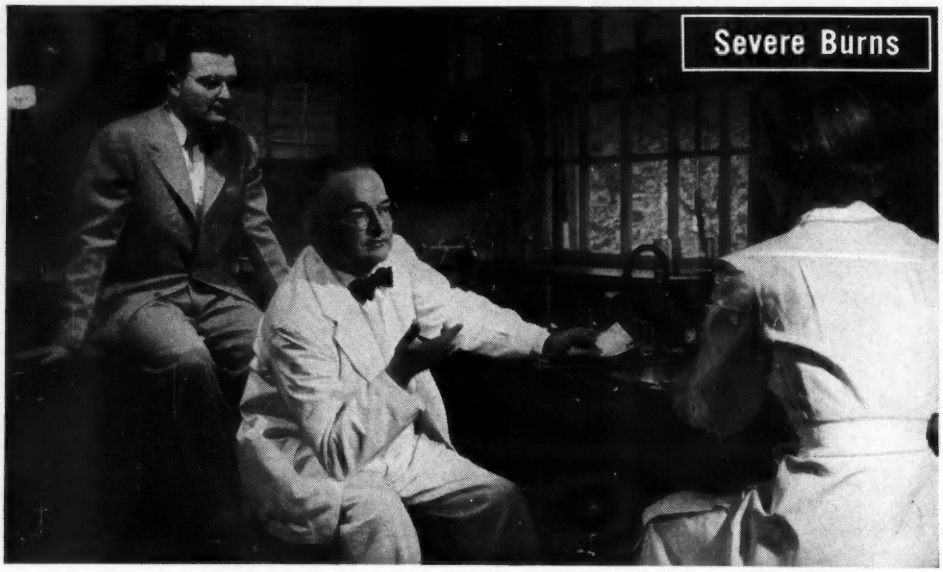
OFFICIAL JOURNAL
OF THE CALIFORNIA MEDICAL ASSOCIATION

VOLUME 75 NUMBER 4



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*Whitelaw, M. J., J.A.M.A. *145:* 85, Jan. 13, 1951.

California MEDICINE

OFFICIAL JOURNAL OF THE CALIFORNIA MEDICAL ASSOCIATION
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VOL. 75 OCTOBER 1951 No. 4

Specialist-General Practitioner Cooperation in an Obstetrical Department

BLAKE H. WATSON, M.D., *Los Angeles*

SUMMARY

At a private hospital not affiliated with a teaching institution, a system was set up in the obstetrical department under which general practitioners carrying out deliveries had the advice and aid of specialists in obstetrics and were required to call for it in stated circumstances. General practitioners carried out about half of the 17,076 deliveries at the hospital in an eight-year period. Teamwork was stressed. Results were comparable with those reported from many of the well-known institutions.

In addition, a special anesthetic service was organized for the obstetrical department. Anesthesia was administered by young physicians who not only were versed in anesthetic procedures but had special training in obstetrics.

The service was available at any hour, and the physician carrying out delivery could count upon competently administered anesthesia when it was needed, as well as upon consultation and assistance should the need arise.

SINCE the obstetrical department of St. John's Hospital, Los Angeles, admitted its first patient in November 1942, there have been some 17,000 deliveries. About half of the patients were admitted under the care of general practitioners.

Chairman of obstetrical department, St. John's Hospital, Los Angeles.

Presented before the Section on Obstetrics and Gynecology at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

The data in the accompanying tables indicate the various methods of treatment used and the results. The incidence of various abnormalities was quite similar to that reported from many of the well-known institutions of the country. The ultimate end results in terms of maternal mortality, maternal morbidity, stillbirths, and neonatal deaths compare most favorably with results in the better known teaching and private hospitals where practice is entirely confined to physicians qualified under the term "obstetrical specialists."

Under the heading "Supervision" in Paragraph 5 of "The Minimum Standard for Obstetrical Department in Hospitals"—as demanded by the American College of Surgeons—appears the following requirement: "The obstetrical division of the medical staff shall be so organized as to exercise adequate control over the obstetrical work done in the hospital, such organization to include a chief or head of the department or service who shall be responsible for the general supervision of the professional activities of the department."

In order to exercise adequate control, the quality of work done by each physician engaged in the practice of obstetrics in the department must be known. Therefore, at St. John's Hospital all were classified into two major groups. This classification was arrived at after careful examination of creden-

TABLE 1.—*Presentation and Positions in 17,076 Deliveries*

Vertex		
a. Occiput anterior	14,820	(85%)
b. Occiput posterior	1,410	(8%)
Breech	636	(3.7%)
Brow	16	
Face	30	
Transverse	18	

TABLE 2.—*Method of Delivery*

Total	17,076
Spontaneous	10,264
Low-forceps	4,576
Mid-forceps	97
High-forceps	4
Manual rotation with forceps (mid and low)	530
Forceps rotation with extraction	213
Craniotomy	2
Podalic version and extraction	37
Cesarean section	891
Breech	636

TABLE 3.—*Data on Breech Deliveries (524 Consecutive Cases, Jan. 1, 1943, to Dec. 31, 1949)*

Total number deliveries	14,229	
Total number breech deliveries	524 or	3.68%
Type of Delivery	No.	Per Cent
Decomposition of breech and extraction	32	6.1
Spontaneous with breech assistance	440	83.9
Cesarean section	52	10.0
Forceps to after-coming head	35	6.6
Maternal morbidity	17	3.2
Fetal mortality (uncorrected)	80	15.2
Fetal mortality (corrected)	7	1.3
Maternal mortality		None

tials bearing details of training, practical experience and qualification by major obstetrical boards. This was followed by personal observation of the individual's handling of normal and abnormal procedures in the department itself and his ability as demonstrated during this period of probation.

Group A consisted of physicians permitted to carry out all types of obstetrical procedures, consultation being required only in cases of cesarean section. This group included all qualified obstetricians.

Group B consisted of physicians permitted to practice obstetrics in the department but restricted to cases in which the delivery was normal and uncomplicated. Should complications arise, one of the consulting staff must be called in to aid in the conduct of the case wherever possible or, if necessary, take over until safe delivery is accomplished.

The physicians in Group B are required to call for consultation:

1. Prior to any obstetrical operation, with the exception of episiotomy or prophylactic use of low forceps.

2. For induction of labor by the use of pituitary extract or rupture of the membranes.

3. In any case in which the patient has been over 12 hours in active labor or in which the membranes have been ruptured for 12 hours.

4. In all cases of toxemia.

5. In any case in which the patient is admitted with evidence of bleeding, before, during or after parturition.

6. In any case of abnormal presentation, including primiparous breech.

7. Prior to cesarean sections.

8. In any case of postpartum complication such as pyrexia, thrombophlebitis, etc.

This consultation service was provided by a group, designated as obstetrical consultants, appointed by the obstetrical committee. The consultants gave their service free of charge to the patient as a service for better obstetrics, except in instances in which the attending physician advised that a fee should be charged.

In approximately 95 per cent of cases, consultation was gratis.

Consultants have been encouraged to attempt close relationship with the general practitioners in this supervisory and consultant capacity. The aim has been to impart a general feeling of working as a team for the good of the patient and to avoid any implication that the consultant is trying to steal the glory and the patient from the practitioner who admitted the patient to the department. Following cesarean section, the general practitioner is encouraged to carry out the daily postpartum care, although the operating surgeon must also continue observation and daily visits. Standard techniques for labor and delivery room, to be followed by all physicians and the nursing staff, were set up and posted.

Luncheons which all physicians doing obstetrics are urged to attend are held monthly. A detailed obstetrical report is available to each physician attending. The report contains data on the following: Presentation and position; lacerations; anesthesia (type used); toxemia; prolonged labor; type of de-

TABLE 4.—*Cesarean Sections*

	Total	Repeat	Incidence (Per Cent)
1943	57	7	3.3
1944	81	12	4.5
1945	89	13	5.1
1946	115	16	6.0
1947	133	37	5.6
1948	120	24	5.3
1949	133	41	5.8
1950	132	38	5.4
	860	188	4.8

Deaths, 2 (2.3 per cent)

TABLE 5.—*Data on Stillbirths*

	Total	Under 30 Weeks	Under 36 Weeks	Full Term
1943	23	10	4	9
1944	21	10	5	6
1945	24	8	3	14
1946	30	12	5	13
1947	26	13	2	11
1948	26	10	5	11
1949	27	9	6	12
1950	29	12	8	9
	206 (1.2%)	84 (0.5%)	38 (0.2%)	85 (0.52%)

TABLE 6.—*Neonatal Deaths*

	Total	Under 30 Weeks	Under 36 Weeks	Full Term
1943	22	9	5	8
1944	24	6	9	9
1945	25	8	12	3
1946	37	23	5	9
1947	31	21	1	9
1948	31	19	5	7
1949	34	16	4	6
1950	24	10	6	8
	228 (1.28%)	112 (0.7%)	47 (0.3%)	59 (0.4%)

TABLE 7.—*Maternal Mortality*

1943	0
1944	0
1945	3
1946	0
1947	1
1948	1
1949	2
1950	0
	7 (0.04%)

livery; episiotomy; spinal anesthesia; hemorrhages; tumors associated with pregnancy. A summary of all cesarean sections, stillbirths, neonatal deaths and maternal deaths is carefully prepared by the resident. Free discussion is encouraged and criticism is welcomed. Reports on interesting cases taken only from the department are presented and discussed. Specialists in other fields, such as internists and radiologists, are invited to correlate factors relating to their specialties with the case in question.

OBSTETRICAL ANESTHESIA

During the first three years of this program, obstetrical anesthesia was administered by the Sisters and by nurses. Not all of them were well trained in the art of anesthesia. With the introduction of spinal block, it was imperative that trained anesthesiologists be introduced into the department. (The author is of the opinion that spinal anesthesia should not be administered by the attending physician, because as he must leave the head of the table to carry out the delivery, he cannot constantly observe the patient for changes in blood pressure and respiratory rate, vomiting, etc. This opens the door to accidents which are avoidable if careful observation is maintained.) The department of anesthesia was approached, but for many reasons a working regime could not be guaranteed at all times. For this reason, a branch of obstetrical anesthesia was formed in the obstetrical department. Four young qualified obstetricians, all of whom had given obstetrical anesthetics in many cases, were chosen. One of them had administered caudal anesthesia in over a thousand cases. (Caudal anesthesia is not encouraged in the department of anesthesia in this hospital.) All of them had an intense interest in obstetrics and none of them was so well established in private practice that he could not devote a good deal of time to the assignment. With this nucleus, all anesthesia given in the obstetrical department was administered by trained men. It was required that one of these men be on duty in the hospital at all times. The four physicians with whom the service was begun have in turn trained other young qualified physicians. It is hoped that by following this course the system can be continued until something more satisfactory can be achieved. These physicians who administer the anesthesia are paid for their services on an individual fee basis, for which the patient is responsible.

The system outlined has an important place in the obstetrician-general practitioner team. Not only does it provide well administered anesthesia, but in times of emergency there is at hand a well trained, qualified obstetrician who can give help when it is needed, advice when it is desired, and if necessary can take over the delivery. In many cases in which complications such as prolapse of the cord or terminal abruptio placentae occurred, the presence of an experienced obstetrician has been of great benefit. Moreover, it is reassuring to know that, in case of hemorrhage or shock, a physician experienced in the proper therapy in the form of plasma, blood, oxygen, etc., is standing by. The aid of physicians with knowledge of resuscitation of the newborn and of endotracheal catheterization has prevented infant deaths on many occasions. The constant presence of an experienced obstetrician in the confines of the obstetrical department is also a comfort to members of the attending nursing, resident and intern staff who may seek his counsel in event of complications.

It is the duty of physicians, whether obstetricians

TABLE 8.—*Causes of Maternal Death*

1. Toxemia of pregnancy (acute yellow atrophy).
2. Toxemia of pregnancy (eclampsia with cerebral accident).
3. Cardiac disease in pregnancy (acute right-sided heart failure).
4. Postpartum air embolism (spontaneous delivery).
5. Toxemia of pregnancy (eclampsia—generalized arteriosclerosis).
6. Cardiac death intrapartum (coronary spasm due to ergotrate given intravenously).
7. Prepartum cerebral vascular accident (thrombosis sagittal sinus). Postmortem cesarean section successful.

TABLE 9.—*Obstetrical Anesthesia*

Year	Total Deliveries	Anesthesia Employed: Inhalation No.	Inhalation Pct.	Spinal No.	Spinal Pct.	Miscellaneous
1943	1,722	1,711	(99.36)	9	(00.36)	2 pentothal, 5 none
1944	1,781	1,769	(99.32)	3	(00.34)	3 none
1945	1,710	1,689	(98.77)	19	(1.2)	2 caudal
1946	1,911	1,504	(78.70)	402	(21.03)	2 caudal, 3 none
1947	2,336	1,079	(46.19)	1,249	(53.47)	8 none
1948	2,252	1,070	(47.51)	1,168	(51.86)	14 none
1949	2,300	1,154	(50.20)	1,123	(48.80)	1 local, 22 none
1950 (Through June)	1,138	574	(50.50)	555	(48.70)	1 local, 8 none

or general practitioners, who care for parturient women, to do their utmost to deliver a healthy infant without damage to the child or to the mother. It is consistent with this duty to seek and to give help and advice and to pool knowledge in a common effort to perform good safe obstetrics. In doing so lies hope for nearly perfect results.

10962 Le Conte Avenue.

Discussion by ROBERT H. FAGAN, M.D., *Beverly Hills*

With regard to Dr. Watson's paper, there are three points that I feel could bear even further emphasis: First, the fact that the statistics are from a non-teaching hospital. Second, the fact that 50 per cent of the cases were managed by general practitioners. Last, Dr. Watson's system of providing obstetric anesthetists—a system which I, as an attending obstetrician, have found gratifying and practical.

Formerly, statistics such as these occurred only in teaching hospitals where the standards of medical care have been traditionally high. In recent years, reports from private hospitals all over the country show similarly remarkable records. This is an admirable transition, for obviously not every hospital can be associated with a medical school and, when records such as these occur, we may feel assured that better medical care is becoming more universal and is not necessarily limited to the so-called "fountains of learning." As a matter of fact, because teaching hospitals must necessarily be ultra-conservative, many advances in obstetric procedures now arise in the private institutions. However, in the comparison of mortality statistics, one must remember, in fairness to all, that many teaching and general hospitals have large indigent clienteles, where malnutrition, poverty and lack of cooperation of patients augment obstetrical disasters.

The fact that 50 per cent of the deliveries in St. John's Hospital were managed by general practitioners is interesting and tends to support the general trend in medical education that there is a need for general practitioners, even in large metropolitan areas. The over-all obstetrical care in a community may be improved by making arrangements for general practitioners to work in cooperation with the obstetrical specialists in hospitals where consultation and help in emergencies is readily at hand. In hospitals lacking this supervision, results are not so favorable.

Probably there has been no factor in obstetrics so unsatisfactory as being unable to procure hurriedly at all times a good obstetric anesthetist. I believe it is understandable that certified anesthetists should choose not to give obstetric anesthesia because of the long and uncertain hours. The procedure at St. John's as outlined by Dr. Watson is one of the most gratifying arrangements that I have experienced in over 20 years of obstetric practice. The realization that there is constantly available a physician well trained in obstetrics, as well as in obstetric anesthesia, affords to all concerned great security in emergencies.

These obstetrician-anesthetists must be qualified in various techniques of obstetric anesthesia and this ability may be and should be acquired, in my opinion, by all obstetricians during their hospital training. In addition to the obvious advantages to the patients, the nurses and the attending physicians, the benefits to these young men are very great. They profit greatly by observing the conduct of labor of their older confreres. One of the unfortunate aspects of obstetric practice is that often after a physician leaves his formal training he never again observes a colleague conduct a delivery. It is amazing how many variations in procedures are improvements over the techniques one has originally acquired, and it is by the observation of a large number of competent obstetricians at work that younger men may ultimately perfect the techniques of delivery best adapted to their own capabilities. Moreover, the first few years of obstetric practice are necessarily lean ones financially, for in contradistinction to other branches of medicine, the young obstetrician has no available insurance work or industrial contracts which help a young physician pay his overhead. The fees that may be charged for obstetric anesthesia, therefore, are most welcome. The patients, the delivery room personnel, the attending physicians and the younger physicians all profit. As far as I can see, there are no objections to this arrangement. I heartily commend it as the most satisfactory method of handling this major obstetrical problem that I have personally observed. I believe Dr. Watson and the personnel of St. John's Hospital are to be congratulated for the excellent record they have established.

The Treatment of Metastatic Breast Cancer in Bone

MERRELL A. SISSON, M.D., and L. H. GARLAND, M.D., *San Francisco*

SUMMARY

The authors report clinical experience with 212 cases of mammary cancer metastatic to bone, in 186 of which radiotherapy was given, and in 26 steroid hormone therapy.

At least 70 per cent of patients with bone metastasis from breast cancer were relieved of pain by adequate roentgen therapy, the relief lasting for most of the survival time in many instances.

About 25 per cent of patients had recalcification or reossification of bony lesions with roentgen therapy; while dramatic, this is not always an indication that relief of pain will continue or that survival time will be lengthened.

If and when adequate radiotherapy has not been effective or cannot be administered (for example, in a patient with extremely widespread metastasis, or one residing at a considerable distance from radiotherapeutic service) steroid hormone therapy in adequate dosage is frequently beneficial. From 40 per cent to 75 per cent of patients with bone metastases from breast cancer are relieved of pain by steroid hormone therapy. In about 15 per cent of cases recalcification of the lesion occurs.

Effective roentgen therapy may usually be given in a relatively brief period of time (one to two weeks). Effective steroid hormone therapy usually requires from 12 to 24 weeks.

Complications of steroid hormone therapy are numerous. Some patients are made considerably worse by such therapy. These complications may only be controlled by reduction or discontinuation of the hormones. For this reason, it is recommended that irradiation always be used as the initial method of palliation.

IN an extensive review of the present status of cancer chemotherapy published some months ago, Karnofsky and Burchenal[15] made this pertinent observation: "The tremendous interest in the chemotherapy of cancer is out of proportion to the practical contributions that chemotherapy thus far has made to the management of the disease." Although this "tremendous interest" is of great importance, it has tended to obscure the fact that for one type of cancer, namely, mammary cancer metastatic to bone, there is a simple and effective method of therapy available in most communities in this country. In order to review the experience of the authors in this field, and to present comparative results in a series of cases treated respectively by radiotherapy and steroid hormone therapy, this paper is being presented.

Breast cancer is the commonest form of malignant tumor in females; the incidence is about 60 per 100,000 women, per annum, in one sector of this country. Since many of its victims live for long periods of time, the prevalence of the disease is probably five-fold the incidence figure. Haagensen[13] estimated that the disease develops in 4 per cent of adult women.

From the Departments of Radiology, Stanford University Hospital, San Francisco Hospitals, and St. Joseph's Hospital, San Francisco.

Presented before the Section on Radiology at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

The incidence of bone metastasis varies with the duration of the disease, the success of initial treatment of the primary lesion, and the method of examination used in the detection of metastases. Bone metastasis has been reported in about 75 per cent of cases at autopsy by different observers.[1,9] In a series of 886 cases of breast cancer, mostly recurrent or inoperable, recently studied by the Collaborating Investigators on the Subcommittee on Steroids of the American Medical Association Committee on Research,[8] there were demonstrable bone lesions in slightly over 55 per cent. In a study of 767 cases of "operable" breast cancer (all patients subjected to radical mastectomy) Nohrman[19] found that even in this relatively favorable group bone metastases developed within ten years in 28 per cent of the patients (see Table 1). In the authors' clinical experience, bone lesions developed in at least 50 per cent of patients not initially cured of breast tumor.

On the basis of an extensive review of cases at the Mayo Clinic, Burch[5] concluded that the greater

TABLE 1. — *Incidence of Skeletal Metastases After Radical Mastectomy (767 Patients)* (Nohrman)

Clinical Stage of Primary Tumor	Bone Metastasis Occurrence Within 5 Years	10 Years
Stage I	10%	15%
Stage II	27%	37.3%

the degree of axillary node involvement, or the younger the patient, the earlier was the occurrence of metastasis.

About 95 per cent of metastatic bone lesions produce pain at some time during their course. Pathologic fractures develop in many such lesions, notably in the ribs, vertebral bodies and other weight-bearing bones. Severe anemia develops in some cases, and hypercalcemia in a few, especially in those patients with generalized skeletal involvement who are confined to bed.

The metastatic lesions are osteolytic in about 75 per cent of cases, osteoblastic in about 10 per cent, and of mixed type in the remaining 15 per cent. When the cortex of a bone is involved, an osteolytic lesion larger than 5 mm. can usually be detected by proper roentgenologic examination. However, when the medulla alone is involved, there may be extensive deposits that are not observable in roentgenograms. For this reason, it is wise to treat patients with clinical evidence of metastatic bone lesions even though the presence of the lesion cannot be confirmed roentgenographically.

DIAGNOSTIC PROCEDURES

In addition to the usual history and physical examination, plus roentgenograms of the area in which patient complains of pain, it is desirable in many cases to have a simple or basic skeletal survey, plus a few laboratory determinations, especially if steroid therapy is contemplated. A basic "x-ray survey" is regarded as:

1. Skull (posterior-anterior and lateral films).
2. Chest (posterior-anterior and lateral films).
3. Lumbosacral spine and pelvis (anterior-posterior and lateral films).

Stereoscopic studies tend to enhance the value of the above projections, especially in cases of questionable or small lesions.

Basic clinical laboratory determinations include blood cell count and hemoglobin and serum calcium determinations. The importance of the latter cannot be overstressed in the event that steroid hormone therapy is undertaken, since serious hypercalcemia may be present or develop during such therapy, especially in patients confined to bed. Too frequently in such circumstances the symptoms are attributed to bowel obstruction, brain metastases or uremia. Swyer and co-workers[24] recently reported hypercalcemia in 14 per cent of a group of patients observed, all apparently prior to treatment. The main triad of changes in this hypercalcemic syndrome are (1) gastrointestinal disturbances (anorexia, nausea and vomiting); (2) mental changes (incoherence, speech difficulty, apathy and even coma); and (3) renal impairment (gradually decreasing urinary output, with increase in the blood urea nitrogen).

TREATMENT

The treatment of metastatic cancer in bone is essentially palliative, and directed toward the relief of pain or the healing of fractures. It may be in the form of radiotherapy, steroid hormone therapy, and, perhaps, alternation or combination of the two methods. In most cases, with judicious treatment, life is made more comfortable and in some it is prolonged. It is essential that simple measures precede or be combined with specific treatment, notably measures to improve the general nutritional status of the patient, especially as regards adequate protein and vitamin intake.

Radiotherapy may be given by external roentgen therapy, external radium therapy or internal irradiation (radioactive isotopes). The simplest, most effective and most easily controlled method is external roentgen therapy. A majority of patients treated by the authors were given 200-kilovolt irradiation, using a half-value-layer of approximately 1.0 mm. copper a target-skin distance of from 50 to 80 cm., and fields large enough for the lesion or lesions under treatment. Since microscopic involvement of bone often exists alongside macroscopic, and since the relative depth dose of 200-kilovolt irradiation is much greater when large areas are irradiated, the fields commonly used ranged from 15 cm. up to 30 cm. in diameter. The initial course usually consisted of a series of treatments given over a period of one to two weeks, to deliver a tumor dose of from 500 to 1,000 r. The daily doses ranged from 100 to 200 r, measured in air, usually to one field. In about 80 per cent of cases there was significant relief of pain during or within a few weeks of the end of this course. If relief of pain was inadequate or of short duration, a second course was given, equal in amount to the initial one. When and if pain recurred in the same or other sites, additional such courses were given, over a period of years if necessary.

Radium therapy has been used by a few workers, chiefly in the form of teleradium, but is not generally regarded as a practical method of therapy. Gamma-ray cannons using radioactive cobalt slugs fall in the same category, at least at present.

Internal irradiation by means of radioactive phosphorus was used in a small group of cases reported by Friedell and co-workers.[10] The duration of life after treatment in the 12 patients given radioactive phosphorus averaged 5.4 months. Pain relief of moderate degree occurred in most of them, but was vitiated by complications secondary to damage of the hematopoietic system; severe hemorrhagic tendencies occurred nine times in 14 courses of treatment.

Hormonal therapy is designed to alter the environment of hormonally dependent cells, rather than directly destroy or suppress the cells (as radiation attempts to do). Hormonal imbalance may be obtained by surgical or radiological castration, by autocastration (in the case of those patients with metastasis to the ovaries), and by the administration of suitable steroid hormones.

Surgical or radiological castration (without added

local treatment to the extra-pelvic osseous metastases) will sometimes induce a striking remission of generalized bone lesions. Unfortunately, this striking effect occurs in only about 20 per cent of cases, and cannot be predicted in advance. Furthermore, the method is, of course, applicable only to premenopausal patients.

Creation of hormonal alterations by administration of androgens to women in the younger age group (mostly under 55) and estrogens to those over that age is frequently successful in the relief of pain and occasionally in the recalcification of osteolytic bone lesions. If patients do not respond to one type of hormone (e.g., estrogens) it may be possible to obtain remission with the opposite type. Such reversal of hormone balance may be successful on more than one occasion in a few cases. However, not many patients survive long enough for thorough use of alternating hormone therapy.[6]

Cortical steroids have been tried in a few cases of metastatic mammary carcinoma. Taylor and coworkers[25] reported five cases in which patients with advanced breast cancer were treated with pituitary adrenocorticotropic hormone and cortisone. A carcinomatous ulcer healed in one case, a skin nodule decreased in size in another. The behavior of such bony metastases as were present was not specifically commented upon.

RESULTS OF ROENTGEN THERAPY

In collaboration with Picard and Baker, the authors recently reviewed in some detail the results of x-ray treatment in 79 cases of mammary cancer metastatic to bone, all followed to death.[12] These results may be summarized as follows: 68 per cent of the patients obtained satisfactory or complete pain relief; 32 per cent obtained little or no benefit. Slightly over one-half of the patients had relief of pain for most or all of their survival time. The average survival time for the group as a whole was 12 months from the development of roentgen evidence of bone metastasis. These results are contrasted with those of other investigators in Table 2.

In approximately one-half of the 79 cases reviewed, adequate serial roentgenograms were available for study. In 26 per cent of these cases, recalcification or reossification of the metastatic bone lesions was apparent (that is, previously osteolytic foci filled in or previously osteoblastic foci restored to normal architecture). In somewhat over one-third of the cases there was no change in the appearance of the metastases during a time interval of some three to 12 months; this apparent arrest in progression was noteworthy in some cases. In the remaining patients, that is, about one-third of the group, there was steady progression of the metastatic bone disease. These results in recalcifying the lesion may be compared with those reported by others in Table 3.

TABLE 2.—*Results of Roentgen Therapy of Bone Metastases from Cancer of the Breast*

Author	No. of Cases	Per Cent Pain Relief	Average Survival Period (After Discovery of Bone Metastasis)
Wulff	44	46	14.3 months
Bouchard	23	65	13.6 "
Pohle and Benson	18	65	..... "
Burch	41	70.6	15.5 "
Lenz and Freid	31	71	11 "
Deucher	145	78	13 "
Leddy, et al.	106	80	..... "
Garland, et al.	79	68.4	12 "

TABLE 3.—*Recalcification of Bone Metastases Following Roentgen Therapy*

Author	Cases	Per Cent
Wulff	44	22.7
Bouchard	23	26
Lenz and Freid	27	37
Garland et al.	38	26.3

In addition to the previously mentioned group of 79 patients, the authors treated 107 patients with bone metastasis from breast cancer in private practice, both office and hospital. Some of these patients are still under treatment, some have died after varying periods of relief, and some are untraced. Clinical records indicate that the percentage of patients with relief of pain was somewhat higher than in the first reported group, but in the absence of complete follow-up data, the average duration of this favorable response cannot be stated. The number of cases in which adequate serial roentgenograms were available was not large enough to warrant analysis with regard to the proportion of patients who had objective improvement. Many patients with relief of symptoms do not return for follow-up films.

RESULTS OF STEROID HORMONE THERAPY

The author studied a small group of 20 cases in which the patients were treated with steroid hormones in accordance with the program of the Committee on Research of the American Medical Association.[12] About 40 per cent of the patients given androgen treatment had relief of pain, but none recalcification. About 33 per cent of estrogen-treated patients obtained relief, and one of six had recalcification. In a large group of cases studied by the Collaborating Investigators, the incidence of relief of pain in the androgen-treated group was considerably higher than it was in the author's corresponding group, but in the estrogen-treated group was quite similar. The mean survival time in the larger group of steroid hormone-treated patients was 8.8 months, as contrasted with the authors' experience of 12 months with roentgen therapy.

Results of Garland and co-workers with the use of steroid hormones are compared with those of other groups in Table 4.

Subsequent analyses have shown that the objective bone response in patients over 50 years of age was considerably better than that in the group under 50. This applied to both androgenic and estrogenic therapy.

In addition to the initial group of 20 patients

TABLE 4.—*Effect of Steroid Hormone Therapy (Androgenic) on Bone Metastases from Cancer of the Breast (Garland et al.)*[12]

Author	Cases	Subjective Relief (Per Cent)	Objective Change (Recalcification by X-Ray) (Per Cent)
Van Winkle, 1949	77	45	13
Andersen, 1949	21	58	19
Adair et al., 1949	48	75	19
Nathanson, 1949	65	83	24
Garland et al., 1950	9	40	0
Van Winkle (Committee on Research), 1950	218	75	16

given steroid hormone therapy (previously reported[12]) six others have been treated. The results were essentially the same as in the earlier group. A few were given a trial of associated roentgen therapy; on these no conclusions are yet warranted.

COMMENTS ON DOSAGE AND SIDE REACTIONS

Roentgen therapy. The optimum radiotherapeutic dose for skeletal metastases has been a subject of considerable discussion ever since Freund[11] first reported the results of such treatment in 1907. Many radiologists prefer small to moderate doses (for example, 600 to 1,000 r estimated in the tumor in six to 12 days) while others advise heavy irradiation (3,000 to 5,000 r in the tumor in 15 to 30 days). It has been the authors' experience, based on some 214 cases, that the vast majority of patients get relief of pain and that in some cases there is roentgenographic evidence of recalcification after small doses—for example, 600 r into the metastatic tumor area. If relief should not be obtained within a few weeks of the initial course, additional dosage should be given. These small courses may be repeated safely up to four or five times during the lifetime of the average patient with metastatic mammary carcinoma in the event that the lesions recur or new lesions develop in adjacent areas.

Wulff,[28] Peck, Ransom and Hodges,[21] Burch,[5] Leddy and Desjardins,[16] Pohle and Benson[22] and others[17] also recommended moderate dosage, Wulff observing that "large and intensive series of treatments seem if anything to do more harm than good."

On the other hand, Paterson[20] advised as much as 1,000 to 1,500 r in one *day*, or "2,500 r tumor in eight days," for localized deposits. Freid and Goldberg[9] advised a dose "up to 3,000 r per field over several fields." Bouchard[4] gave from "2,000 to 4,000 r air."

It seems probable, in retrospect, that some of the authors' own failures in obtaining relief of pain were due to not following up the initial course of irradiation with a second one after an interval of three or four weeks. Supplemental protein administration was rarely attempted; in the light of recent concepts of bone regeneration it should prove helpful in some cases.[23]

Complications and side effects. The immediate complications of properly given roentgen therapy (for bony metastases) are either nil or consist of mild nausea. In the doses the authors employ, skin erythema or increased bone pain does not occur. Temporary epilation follows treatment of cranial metastases. In premenopausal women, pelvic irradiation is naturally and fortunately followed by amenorrhea. Any symptoms from this "artificial menopause" tend to be in direct ratio to the advance impressions given to the patient; they are negligible in psychologically prepared or mentally stable patients. If roentgen dosage to an abdominal field is unduly heavy, the complications of course include severe nausea, vomiting, erythema, accentuation of pain and so forth.

Steroid hormone therapy. The optimum dosage of androgenic substances is being studied by the investigators of the Subcommittee on Steroids and Cancer. Their work to date suggests that a dosage of 150 mg. of testosterone propionate per week for 12 or more weeks may be optimal. However, the evidence to date does not prove that any one dosage schedule (e.g., 75, 150, 300 or 600 mg. per week) is definitely superior. Before concluding that a patient will not respond to testosterone a total dose of at least 3 gm. and a duration period of at least three months is desirable. This "full course" of treatment is advisable even if symptoms respond in a shorter period. The principal field of usefulness of androgens appears to be in premenopausal women; bone metastases in postmenopausal women appear to respond equally well to either hormone.

The optimum daily dosage of estrogenic substance is not known. The Subcommittee's investigators on estrogens have included a study of several preparations, each at a certain daily dosage, with the use of diethylstilbestrol as a "standard" for comparison. The minimal effective total dose of diethylstilbestrol, Premarin,® Dienestrol® and DMS (dimethyl ether of diethylstilbestrol) is about 4 gm., and the minimal length of treatment about six months. The minimal total dose of ethinylestradiol and estradiol dipropionate is 200 to 500 mg. and the minimum length of treatment also about six months.

Investigations of other compounds, such as TACE (tri-para-anisyl chloroethylene) methylandrostenediol and methyl testosterone, are being made. Methyl androstenediol is an androgen with less virilizing property than testosterone; Homburger and co-workers[14] reported apparently favorable results with its use in seven cases, but further study is needed.

Complications and side effects. The complications of adequate steroid hormone therapy are relatively common and occasionally fatal. They include hirsutism, edema, uterine bleeding, nausea, vomiting, hypercalcemia and urinary incontinence (see Table 5). Some patients, especially those treated with estrogens, should have curettage to rule out a coexisting or previously silent uterine carcinoma.

Complications are sufficiently frequent to render it advisable almost always to use radiotherapy

rather than hormone therapy as the initial method for palliation.

COMPARATIVE EFFECTIVENESS OF ROENTGEN AND STEROID HORMONE THERAPY

In the authors' experience, roentgen therapy for patients with mammary cancer metastatic to bone resulted in subjective improvement in about 70 per cent of cases and in objective improvement in about 26 per cent. With steroid hormone therapy there was subjective improvement in approximately 40 per cent of cases, and objective improvement was negligible. However, the experience of other investigators with steroid hormone therapy has shown results very comparable to those obtained by the authors with roentgen therapy (see Table 6).

This table does not reflect another comparative advantage of roentgen therapy, namely, apparent longer "arrest" (although not recalcification) of metastatic lesions. In the irradiated cases about 35 per cent of patients had no pronounced progression for a period of three to nine months following treatment, while such apparent arrest occurred in only about 15 per cent of hormone-treated patients.

The mean survival time of all patients receiving roentgen therapy for bone metastasis was 12 months, and of all patients receiving steroid hormone therapy for bone metastasis, 8.8 months. The slight difference in these two figures may be due entirely to the nature of the material in the two groups of cases. Clinically troublesome side effects are more common with hormone therapy than with irradiation, and actual worsening or acceleration of lesions occurs in a small percentage of hormone-treated patients, but in no roentgen-treated patients in the authors' experience.

Numerous investigations are being pursued in an effort to improve the efficiency of hormone therapy, and to study the effectiveness of combining roentgen and hormone therapy. No conclusive results have as yet been published. It has been suggested that ACTH (adrenocorticotropic hormone) or cortisone may be used as a temporary palliative agent in very severe advanced cases, previously not treated by roentgen or hormone therapy, to be followed in due time by one or other of those weapons.

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ACKNOWLEDGMENT

The authors wish to express their deep appreciation to the Subcommittee on Steroids and Cancer (of the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association) for the privilege of taking part in the steroid hormone therapy program, and for the opportunity of reviewing the pooled results of the Collaborating Investigators to date.

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TABLE 5.—*Incidence of Side Effects of Steroid Hormone Therapy*

	With Androgens (Per Cent)	With Estrogens (Per Cent)
Hirsutism	65	....
Edema	29	33
Bleeding	3	26
Nausea	8	33
Vomiting	6	19
Hypercalcemia	8	3
Urinary incontinence	....	10

TABLE 6.—*Comparative Effects of Roentgen and Steroid Hormone Therapy in Breast Cancer Metastatic to Bone (Garland et al.)*[12]

Treatment	Cases	Subjective Improvement (Pain Relief) (Per Cent)	Objective Improvement (Recalcification) (Per Cent)	Clinically Troublesome Side Effects (Per Cent)	Lesions Apparently Made Worse (Per Cent)
Irradiation	79*	68	26	5	0
Androgen	218†	75	16	25	0.7
Estrogen	77†	38	18	15	2.5

* Authors' material.
† Material of the Subcommittee.

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Diagnosis of the Hemolytic Anemias

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SUMMARY

Classification of the varieties of hemolytic anemia is based upon whether hemolysis is due to inherent defects within the erythrocyte or to extracellular factors.

Confirmation of diagnosis in cases in which the disease is clinically suspected is made upon the basis of the following laboratory data: Hyperbilirubinemia giving an indirect van den Bergh reaction, observation of typical factors in a smear of the blood, a reactive bone marrow, increased urobilinogen in stools and urine, and absence of bilirubinuria.

Differentiation of the different types depends upon determination of altered fragility of erythrocytes as indicated by tests of resistance to heat, acid, and mechanical and osmotic stimuli, and upon the identification of an antibody.

The importance of detecting antibodies demonstrable in acid serum is mentioned.

In a majority of cases, acquired hemolytic anemia is caused by antibodies, malignant disease, or toxic agents.

HEMOLYTIC anemia results from an increase above normal in erythrocyte destruction and beyond the compensatory ability of the bone marrow to match.

The average life-span of the normal erythrocyte is about 120 days. This has been conclusively established both in this country and abroad by transfusion experiments involving the introduction into normal persons of normal erythrocytes either tagged with P_{32} or of a different blood group than the blood of the recipient. These transfused erythrocytes may be identified by the Geiger counter or by differential agglutination. There is normal daily destruction and production of 7 to 8 gm. of hemoglobin and about 1 per cent of the circulating erythrocytes. Small increases in erythrocyte destruction may be equalized by increased marrow erythropoiesis, but when destruction outstrips production, anemia results.

The recognition of hemolytic anemia is important because anemia of this order does not respond to iron compounds, liver extract, folic acid, B_{12}, other vitamins, or other hematinics which may be given before the type of anemia is recognized. An accurate diagnosis should always be attempted in order to prognosticate the course of the illness, to avoid useless medication, and also for the very pragmatic therapeutic reason that in a few of the various kinds of hemolytic anemia dramatic results may be achieved by splenectomy or vigorous treatment of the underlying cause. Increased hemolysis may be caused by such diverse mechanisms as splenic destruction of spherocytes, perverse antibody production, leukemia and lymphoma, animal toxins, and chemical idiosyncrasy, to mention a few. Before classifying the hemolytic anemias, the recognition of abnormal hemolysis itself is necessary.

The purpose of this presentation is to state general principles and outline procedures which may be done in the average clinical laboratory. Complete techniques are given in detail by Ham[12, 13] in two recent publications.

In a carefully taken history and physical examination, anemia, icterus, splenomegaly, hepatomegaly, lymphadenopathy, leg ulcers, Raynaud-like phenomena, familial or past history of jaundice, contact with chemicals, or disease not infrequently associated with increased hemolysis will be noted. Clinical laboratory data are usually necessary to confirm the clinical impression and to differentiate between the different groups of hemolytic anemia.

RECOGNITION OF INCREASED HEMOLYSIS

Pigment reactions. Hemoglobin is broken down by the cells of the reticuloendothelial system to the pigment bilirubinglobin. This pigment does not pass the renal barrier, so it does not appear in the urine. It gives the indirect or delayed van den Bergh reaction. The parenchymal cells of the liver split off the globin molecule and excrete the resulting bilirubinate as the sodium salt into the bile, by which medium it reaches the intestines. The bacterial flora of the bowel reduce the bilirubin to the colorless chromogen urobilinogen, part of which is excreted in the feces, the rest being absorbed into the portal circulation. The greater portion is reexcreted in the bile or metabolized by the liver; small amounts are excreted in the urine. An increase in hemoglobin catabolism, therefore, results in an increase in serum bilirubinglobin, fecal bilirubin, and fecal and urinary urobilinogen.[22, 23]

The relative levels of serum bilirubinglobin and fecal urobilinogen are dependent upon the functional capacity of the liver. For example, in moderate hemolytic anemia with good liver function, there may be little or no increase in the icteric index or serum bilirubin, yet the fecal and urinary urobilinogen may be increased to several times normal. On the other hand, a person with a milder hemolytic

Presented before the Section on General Medicine at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

anemia but with impaired liver function may have elevated serum bilirubin. The serum bilirubin alone is therefore not a reliable index of the degree of hemolysis.

Obstructive or hepatocellular jaundice produces increased serum bilirubin, which, unlike bilirubinglobin, appears in the urine and gives a positive direct or immediate van den Bergh reaction. Both bilirubin and bilirubinglobin give a similar icteric index and total bilirubin determination. Demonstration of the absence of bile in the urine will usually differentiate hemolytic from the other types of jaundice. Of the many tests, the best is Harrison's test[9] which employs the precipitation of the bilirubin by barium chloride and its subsequent oxidation to biliverdin by Fouchet's reagent.

The absolute proof of increased hemolysis is the demonstration of increased fecal urobilinogen. To be accurate, the determination should be done on at least a 24-hour specimen or preferably upon the fecal output of four days, the principal method being that of Watson.[24] An increase above 250 mg. in 24 hours is significant. Since not only the rate of hemoglobin destruction but the total mass of hemoglobin is important in determining the excretion of urobilinogen, Miller and Dameshek[14] calculate their hemolytic index as follows:

$$\frac{\text{24-hour fecal urobilinogen in mg. x 100}}{\text{Hemoglobin in gm. per 100 cc. x blood volume} \div 100}$$

The normal index is 11 to 20.

Practically speaking, the determination of 24-hour fecal urobilinogen is not done in most laboratories and the determination upon a single fecal specimen may be misleading. The determination of urobilinogen in a fresh afternoon urine specimen will give a working approximation of the fecal urobilinogen. The method of Wallace and Diamond,[21] which employs the addition of Ehrlich's aldehyde reagent to twofold dilutions of urine, is simple. If a pink color is detected in a dilution of greater than 1:20, the urobilinogen is increased. False low values may obtain if the urine is allowed to stand so that the urobilinogen is oxidized to urobilin or if the oral administration of antibiotics has changed the intestinal flora so that the bilirubin is not reduced to urobilinogen.[10] In porphyria, porphobilinogen will give a positive reaction in high dilution.

Intravascular hemolysis will increase the plasma hemoglobin above the normal 5 mg. per 100 cc. Gross increases may be detected by the pink color of the plasma. Bing and Baker[1] have developed a quantitative benzidine method. It is necessary, of course, to use extreme care in drawing the blood in order not to produce technical hemolysis in the test tube.

The urine should always be tested for hemosiderin. A simple test in which the urine sediment is mixed with an equal part of 30 per cent ammonium sulfide solution has been devised by Cook.[7] The reaction to this test is always positive in nocturnal hemoglobinurina, and frequently in other hemoglobinurias.

Hematological reactions. The erythrocytes vary from normocytic to macrocytic, the degree of macrocytosis being dependent somewhat upon the rapidity of erythrocyte regeneration. Except in Cooley's anemia and uncommonly in sickle-cell anemia in the young, the cells are well filled with hemoglobin. Polychromatophilia and nucleated erythrocytes are roughly proportional to the severity of the anemia and the regenerative ability of the bone marrow. Frequently there is basophilic stippling of the erythrocytes. With severe hemolysis, especially if it occurs intravascularly, fragmented and ghost cells may be observed on the blood smear. In Cooley's anemia and sickle-cell anemia, target cells are present.

Supravital staining with cresyl blue permits counting of the reticulocytes, the best single measure of the physiological activity of the bone marrow. During the regenerative phase following a hemolytic crisis the reticulocytes may number 80 to 90 per cent of the total erythrocytes. A normal reticulocyte count is rare in hemolytic anemia, although Dameshek[7] recently gave examples of acquired hemolytic anemias with low reticulocyte counts before therapy with ACTH. After therapy there was reticulocytosis. (The author has seen one example of this.)

Spherocytes are readily identified on the stained smear by the technician who looks for them. They are to be seen on those well spread portions of the smear where the erythrocytes are neither crenated by the slow drying or excessively spread out. A decreased mean cell diameter with normal mean corpuscular volume and normal mean corpuscular hemoglobin indicates spherocytosis. On a wet mount, spherocytes may be recognized by their rounded shape and inability to form long rouleaux. Spherocytes indicate hemolytic anemia—unless the patient has recently received a blood transfusion. Transfused cells, especially if they have been previously stored, may become spherical. A spherocyte is a congenitally fragile cell or one which has become damaged by some means.

The blood platelets are usually normal unless altered by the underlying cause of the hemolysis.

Unless influenced by the primary condition, the number of leukocytes is normal or often increased with a relative increase in the number of immature neutrophils during acute hemolysis. Evans[8] noted that in certain hemolytic anemias there is thrombocytopenia and neutropenia, suggesting the relationship of these three entities and abnormal antibody formation. Pronounced erythroid hyperplasia occurs in the bone marrow, involving all stages of erythrocyte maturation but especially the pronormoblast phase. A reversed myeloid-erythroid ratio with many pronormoblasts and orthochromatic normoblasts suggests the possibility of hemolytic anemia but bone marrow examination is chiefly of value in ruling out megaloblastic anemia, hypoblastic anemia, and leukemia.

The previously mentioned basic tests on blood, bone marrow, and urine may be done in any clinical laboratory or in the physician's office and the

results will usually establish the presence or absence of hemolytic anemia. The disease may be any of the various kinds in the following classification, and there are means for the specific diagnosis of each kind:

CLASSIFICATION OF THE HEMOLYTIC ANEMIAS

Anemias due to defect in the erythrocyte

1. Congenital hemolytic anemia
2. Sickle-cell anemia
3. Cooley's anemia
4. Congenital nonspherocytic hemolytic anemia (Haden)
5. Nocturnal hemoglobinuria
6. Ovalocytosis with hemolytic anemia
7. Pernicious anemia (the role of hemolysis is a definite although a minor one)

Acquired hemolytic anemias due to causes other than erythrocyte defect

1. Protozoan parasites; malaria
2. Bacterial or animal toxins: *B. Welchii*, snake venom
3. Chemical agents: Chlorates, benzene
4. Thermal burns
5. Intravascular hypotonic solutions: Prostatic resection
6. Symptomatic group: leukemias and lymphomas.
7. Allergic sensitization: Favism
8. Antibody group
   a) Iso-agglutinin reactions: Incompatible blood transfusions, erythroblastosis fetalis
   b) Paroxysmal cold hemoglobinuria (syphilitic)
   c) Anemia due to cold hemagglutinins
   d) Anemia due to "irregular" iso- and auto-hemagglutinins. Most of these were formerly classified as idiopathic acute or chronic hemolytic anemia
9. March hemoglobinuria

Rather than attempt to run through the differential points in the diagnosis of these anemias, special tests of hemolysis and those anemias diagnosed by the tests will be discussed. The order in which the tests should be done is dependent upon the judgment of the clinician. For example, for a young Negro with anemia, the sickle-cell test should be done first. For an older person with a history of red urine and a positive reaction to a Kahn test of the blood, only the Donath-Landsteiner test may be required to establish the diagnosis of paroxysmal cold hemoglobinuria due to syphilis.

SPECIAL DIAGNOSTIC PROCEDURES

Osmotic fragility. An increase in osmotic fragility is present constantly in congenital hemolytic anemia and inconstantly in various kinds of acquired hemolytic anemia. In sickle-cell anemia and Cooley's anemia decreased osmotic fragility occurs. A screen test is done by adding 0.1 ml. of blood to two test-tubes containing 1 ml. of 0.85 per cent and 0.50 per cent of sodium chloride solution respectively.[12] If hemolysis occurs in the 0.50 per cent solution, then further test should be done by Creed's technique[4] which utilizes a series of tubes with saline solution varying from 0.28 per cent to 0.72 per cent with intervals of 0.04 per cent or the more modern quantitative technique utilizing the photoelectric-cell colorimeter.[20]

Detection of antibodies. The antibody-antigen nature of many of the acquired hemolytic anemias was suspected for years. It was impossible, however, using the conventional method of titrating saline erythrocyte suspensions against the suspected serum, to demonstrate agglutination, except in a few instances.

Rh-positive erythrocytes which would be expected to be agglutinated by the serum from sensitized mothers sometimes did not agglutinate. Indeed, the maternal serum from mothers of erythroblastotic children might inhibit the agglutination of Rh-positive cells by serum known to contain saline effective agglutinins. Thus was developed the blocking antibody test which indicated that more than one type of antibody may be responsible for erythroblastosis fetalis.[25]

Wiener, followed by a host of other investigators, showed that substitution of 20 per cent albumin solution (or many other colloidal media) for saline solution would permit the demonstration of antibodies not only in the serum of mothers with erythroblastotic infants but also in the serum of patients with many kinds of acquired hemolytic anemia which had previously been called idiopathic. Thus was born the conglutination test which, in its modifications, is extensively used.[16, 26] The blocking antibody test is little used at present.

Coombs[3] found that the antibodies absorbed on the erythrocytes of babies with erythroblastosis fetalis could not be removed by repeated washing with normal saline solution. He found that serum from rabbits which had been immunized against human globulin would agglutinate these sensitized cells. This is Coombs' test. The next step was the demonstration of a positive reaction to Coombs' test in certain acquired hemolytic anemias.[11] The direct Coombs' test detects only antibodies absorbed on the cell. To detect antibodies in serum, an indirect Coombs' test is employed. Normal red cells of the same group or group O and varying Rh types are incubated with the serum in question and then, after they have been washed, are exposed to Coombs' serum. A quantitative titration of antibodies may be done by the indirect Coombs' technique, thus supplementing the conglutination test.[12]

The Coombs' test is not invariably negative in congenital hemolytic anemia, as was first thought.

An indirect Coombs' titration will generally detect antibodies in higher titre than the conglutination test. Either or both the direct and indirect Coombs' tests may demonstrate antibodies not detectable by other techniques.

Erythrocytes exposed to a solution of trypsin become more readily agglutinable by serum containing antibodies against this particular cell group. Trypsinized cells Rh_1Rh_2 (CDE-CDE) may be used to detect sensitivity to the Rh group antigens. This will provide an extra safeguard for prospective recipients of blood transfusions.[15]

Persons with acquired hemolytic anemia may possess hemagglutinins or hemolysins effective only in an acid medium so that results of a conglutination or indirect Coombs' test may be negative if done in unaltered serum. The acidification of the serum from the patient will detect these antibodies.[15]

Persons with viral pneumonia or with no other disease at all, may develop hemagglutinins which produce erythrocyte agglutination in the cold. The condition should be looked for as the cause in obscure anemia. An alert technician may provide data by which to establish the diagnosis by observing the clumping of the erythrocytes in the counting chamber. These antibodies do not require complement for agglutination. Mechanical agitation of the clumped cells produces hemolysis; this is probably the mechanism in the body where exposure to cold produces intravascular hemolysis and hematuria. Hemosiderin in the urine is commonly found. With high titres, the erythrocytes may clump at a temperature close to that of the body; with low titres, exposure to 4° C. may be necessary. The reaction to the Donath-Landsteiner test is negative.[18, 27]

Syphilitic paroxysmal cold hemoglobinuria is caused by a hemolysin which becomes fixed to the erythrocytes at 4° C. and produces hemolysis when the erythrocytes are then warmed to 37° in the presence of complement. The defect is not in the erythrocyte; the hemolysin will hemolyze normal cells of Group O or of the same blood group as that of the patient. The sensitized but unhemolyzed cells will give a positive reaction to a direct Coombs' test.[12] A person with positive reaction to a serologic test for syphilis who passes red urine after immersion of a limb in ice water may be presumed to have paroxysmal cold hemoglobinuria. Confirmation can be made by the Donath-Landsteiner test which is not difficult to carry out. Caution should be exercised in chilling a patient suspected of having this disease, as excessive chilling may produce a severe systemic reaction with chills, fever, shock, and urticaria as well as the blood in the urine. A person with hemolytic anemia due to cold hemagglutinins, which were previously discussed, may also have blood in the urine after chilling.

Hemolysis at acid pH (Ham's test).[12] In nocturnal hemoglobinuria the erythrocytes have a defect which causes them to be hemolyzed by the patient's or normal serum at an acid pH. The factor present in normal serum which is necessary for hemolysis is heat-labile but is not complement; it may be Ac-globulin.[5] The complete test is time-consuming, as it involves the following 16 combinations:

5 Per Cent Suspension of Erythrocytes from:	Serum		Acidified Serum		Inactivated Serum		Inactivated Serum Plus Complement	
	P*	C*	P	C	P	C	P	C
Patient	±	±	+	+	0	0	0	0
Normal control	0	0	†	0	0	0	0	0

*P=patient; C=control.

†Certain cases of hemolysin or hemagglutinin effective at acid pH will produce hemolysis in this tube.

The complete test is rather time-consuming and if the pH is too low, hemolysis of normal cells may occur. Thus a simple screening test suggested by Ham[12] is useful. Five milliliters of clotted blood from the patient and the same amount from a control are incubated at 37° C. and observed for six and 12 hours. Hemolysis in the tube containing the blood from the patient suggests nocturnal hemoglobinuria, or acquired hemolytic anemia due to an antibody, or sometimes congenital hemolytic anemia; and if that occurs, the complete Ham test must be done.

Detection of sickling. For a long time it has been known that in about 7 per cent of the American Negroes some of the erythrocytes assume a sickle shape when the hemoglobin is in a reduced form. This property is hereditary, being dominant. Pauling[17] observed that the hemoglobin in cells that sickle is of a different molecular weight than normal hemoglobin. The majority of persons in whom this phenomenon occurs have no symptoms but 1 per cent of them have hemolytic anemia with all the characteristics of increased hemolysis. In examination of blood from persons with severe forms of the disease, sickling may be observed on the blood smear or in the counting chamber. This obvious sickling associated with reticulocytosis, leukocytosis, nucleated erythrocytes, and target cells leaves no doubt as to the diagnosis. In the sickle-cell trait and in mild forms of the disease, however, special techniques are required to bring out sickling.

A simple technique has been used for this purpose at the Los Angeles County Hospital. A drop of blood is placed upon a drop of dried cresyl blue on a slide, a cover slip placed over the drop and the edges sealed with vaseline. The preparation is examined at the end of 24 hours for sickling, and at the same time a reticulocyte count is done. Sickling may be demonstrated within 30 minutes by equilibrating the blood with carbon dioxide or by using reducing agents such as sodium metabisulfite.[6]

Mechanical fragility. The measurement of mechanical fragility is not adaptable to the ordinary laboratory. At present the information gained does not warrant its use except in research. The technique is given by Ham.[13]

Miscellaneous conditions. Diagnosis of hemolytic anemia of the symptomatic group depends upon demonstration of an underlying disease known to produce hemolysis. Inconstant spherocytosis, increased osmotic, acid, and mechanical fragility, and a positive reaction to direct Coombs' test[19] may be observed. Hemagglutinins may be inconstantly demonstrated in the serum by the indirect Coombs' test or conglutination test.

There is at the present no practical laboratory test for the confirmation of the diagnosis of Cooley's anemia. A Mediterranean parentage and a blood smear characteristic of thalassemia minor in at least one of the parents will establish the diagnosis.

Hypochromic anemia that is not due to chronic blood loss or infection and which does not respond

to adequate doses of parenteral iron may be Cooley's anemia.

Toxic hemolytic anemia due to chemicals is generally acute. Diagnosis depends upon the exclusion of the other causes of hemolysis and a history of prolonged or extensive exposure to chemicals known to be capable of producing hemolytic anemia. Abrupt onset in persons previously healthy is an important clue. Generally antibodies are not demonstrable.

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Fistulas Following Gastrectomy

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SUMMARY

Postoperative fistula occurred in 16 of 761 cases in which subtotal gastrectomy was done. Twelve of the 16 patients died.

In the majority of cases complications arose because of the anatomical location of the ulcer with surrounding inflammation.

Abrupt and dramatic onset of symptoms following leakage occurred in only a few cases. Perforation occurred in a few cases after the patient had been discharged home well and asymptomatic.

Obstruction of the proximal limb was not present in any of the cases in which postmortem examination was carried out.

The exclusion operation with resection of antral mucosa may not be a safe procedure. For treatment of ulcer which cannot be removed, gastroenterostomy with vagotomy is advised.

SUBTOTAL gastrectomy was done in 761 cases at the University of California Hospital in San Francisco from January 1, 1930, to January 1, 1951. In 16 cases (2.1 per cent) fistulas of the duodenum, antral stump and biliary tract developed postoperatively (Table 1) and 12 of the 16 patients died. Careful analysis of these 16 cases brings out several important points, some of which have not been particularly stressed in the literature.

Clinical Features. Fourteen of the patients were males and two were females. The age range was from 35 to 62 years. In 14 cases the operation was done because of chronic duodenal ulcer, in one because of gastric ulcer, and in one because of prepyloric carcinoma of the stomach. Resection was of the Mayo-Polya type in all cases. Antecolic anastomosis was carried out in five patients, and two deaths occurred. Retrocolic anastomosis was made in 11 patients and ten of them died.

Symptoms. The onset of symptoms indicating intra-abdominal complication of some kind occurred in most patients within the first six days, usually within two to three days, after operation (Table 2). However, three patients had apparently recovered and had been discharged home before untoward symptoms appeared 20 days, 41 days and four months later. The last-mentioned patient had gained 35 pounds and had been feeling well prior to the onset of pain.

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Presented before the Section on General Surgery at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

In only four patients was the onset of intra-abdominal complication abrupt and dramatic in character. Sudden, severe pain was the predominant symptom and was located in the periumbilical or epigastric region, or right or left upper quadrant of the abdomen. Two patients noted radiation of pain to the neck or shoulder region. In spite of immediate operation three of the four patients died. In the remaining 12 patients the onset of symptoms was more gradual, characterized in general by intermittent cramp-like abdominal pain accompanied by increasing distention and absence of peristalsis, increase in pulse rate and variable rise in temperature. In several patients the intra-abdominal complication was completely masked by pulmonary complications or was not recognized until the presence of an abdominal mass or subphrenic abscess became apparent.

Adequacy of Stump Closure. In the earlier cases in the series, duodenal stumps were closed with two layers of continuous catgut followed by a single row of interrupted silk or cotton sutures. Later, the closure was generally made without the continuous catgut. Four patients were known to have a completely adequate duodenal closure since in two patients the primary lesion was in the stomach and in the other two the duodenal ulcer was healed at the time of operation. Death was due to a proven duodenal fistula in both patients with primary stomach lesions.

In the remaining 12 cases a chronic posterior duodenal ulcer was present and dissection was difficult. In four of these 12 cases the ulcer was excluded by dividing the stomach near the pylorus and excising the antral mucosa. Three of these four patients died. In two additional patients fistulas developed following the exclusion operation without

Table 1.—*Fistulas Following Gastrectomy*

Location of Fistula	Number
Antral stump	
With excision of mucosa	4
Without excision of mucosa	2
Duodenum	5
Common duct	2
Biliary drainage, exact source undetermined	3

Table 2.—*Onset of Symptoms*

Time of Onset	Number Patients
Second to sixth postoperative day	13
After hospital discharge	3
20 days; died; duodenal fistula	
41 days; recovered	
4 months; died; antral fistula	

excision of the mucosa and both patients died. In the remaining six patients the ulcers were excised. Dissection was difficult but presumably the closure was considered adequate except in one case in which drains were placed around the stump and brought externally through a stab wound. In that case the patient died following a series of intra-abdominal complications (Table 3).

TABLE 3.—*Adequacy of Stump Closure*

	No. Cases
Excellent	4
2 primary lesions in stomach; 2 deaths 2 duodenal ulcers healed, scarred.	
Ulcer excluded, antral mucosa excised, 3 deaths	4
Ulcer excluded, antral mucosa intact; 2 deaths	2
Difficult, deep posterior penetrating ulcers; 5 deaths	6

Postoperative Complications. Table 4 indicates the secondary operations carried out for the various kinds of complications, and autopsy findings in 10 of the 12 fatal cases. In postmortem examination in eight cases of proven duodenal or antral stump fistula, no evidence of proximal limb obstruction was observed. Perforation occurred in three of four cases in which the antral mucosa had been excised. In two cases injury to the common duct was observed.

DISCUSSION

This study brings out some important points. The incidence of postoperative fistula was higher in patients who had had a retrocolic anastomosis than in those who had had antecolic anastomosis.

TABLE 4.—*Postoperative Complications*

Case	Secondary Operations	Recovered	Autopsy Findings
1	Incision and drainage left subphrenic abscess. (Antral mucosa excised; stump had poor color following first operation.)	Yes	.....
2	Incision and drainage right subphrenic abscess.	No	Duodenal fistula
3	Exploratory laparotomy; no drains. Pancreatitis (?)	No	Duodenal fistula
4	Exploratory laparotomy; drains inserted. Peritonitis. Fistula probably at gastroenteric anastomosis.	Yes	.....
5	Exploratory laparotomy; drains inserted. Peritonitis. Probable duodenal fistula.	No	None
6	Incision and drainage right lower quadrant abscess. Cholecystoenterostomy. Exploratory laparotomy.	No. Complete biliary fistula	None
7	Incision and drainage deep wound abscess. Left subphrenic abscess. Empyema left pleural space.	Yes. Biliary fistula	.....
8	Exploratory laparotomy; drains inserted. Peritonitis. Duodenal fistula.	Yes	.....
9	Exploratory laparotomy. Peritonitis. Drainage. Antral fistula closed with sutures.	No	Antral fistula Antral mucosa not excised
10	Exploratory laparotomy. Peritonitis. Drainage.	No	Common duct fistula
11	Wound drained spontaneously. Peritonitis.	No	Antral fistula Antral mucosa excised
12	Wound drained spontaneously. Peritonitis.	No	Antral fistula Antral mucosa excised
13	None.	No	Antral fistula Antral mucosa excised
14	Exploratory laparotomy; no drains. Peritonitis. Fistula closed with sutures.	No	Antral fistula Antral mucosa not excised
15	None.	No	Duodenal fistula Peritonitis
16	None.	No	Common duct fistula Left subphrenic abscess

This fact in itself may not be too significant, but there are other reasons for favoring the antecolic anastomosis. It is easier to perform, a higher resection can be obtained, and there is less chance for obstruction of the distal limb in an obese person.

Abrupt onset of symptoms was noted in only a few cases. In general, symptoms developed more gradually and in some cases the true nature of the complication was not immediately apparent. Early diagnosis and prompt drainage of the stump area are essential. It is to be noted that leakage of the duodenal or antral stump may occur as a late complication after the patient has been discharged home perfectly well.

The experience in this limited number of cases would indicate that excision of gastric mucosa in antral exclusion operations is not a safe procedure.

The duodenal closure may be difficult following the excision of a deep-seated posterior ulcer. Some factors leading to postoperative leakage in this situation may be inability to obtain a good turn-in, inability of the sutures to hold in the inflamed, edematous tissue, or interference with the blood supply of the duodenum. There was no evidence of obstruction of the proximal limb in any of the postmortem examinations, although this factor was cited by Robinson[3] as the primary cause of duodenal fistulas. Duodenal leakage occurred in four cases in which the duodenum was normal and there was no apparent reason for the leakage.

Peritonitis and its attendant complications caused death relatively early in 11 of the 12 fatal cases. In only one case was there long-standing bile drainage, resulting in the various problems of adequate fluid replacement. The patient, who had a complete biliary fistula, died 63 days after the original operation. In a patient with a long-standing fistula, the precise area of perforation should be determined by the injection of radiopaque media through the external fistula or via the proximal limb of jejunum. The authors believe that when a complete biliary or duodenal fistula is present and persists after a suitable period of observation, an attempt should be made to close the fistula surgically. The operative mortality may be high, but eventually all patients with complete fistula will die if the fistula remains complete.

When a sudden, acute duodenal blowout is suspected, immediate drainage should be instituted through a right subcostal incision. Attempts to close the fistula at this time are usually futile. If possible, some effort should be made to ascertain that the leak has occurred at the duodenal stump, and not at the gastroenteric stoma or in the region of the ligament of Treitz as sometimes happens when there is obstruction of the proximal limb.

The management of a deep-seated posterior duodenal ulcer is often a challenge to the most skillful surgeon. It is often advisable after dissecting down to the region of the ulcer to insert the tip of the index finger of the left hand into the open duodenum and use this as a guide. Perhaps a tube in the common duct, as suggested by Lahey,[2] should be used more often in the deep-seated ulcers that are low in the duodenum. If the stump closure is considered questionable, soft rubber drains should be inserted down to the region of the stump and brought out through a stab wound. In such a situation, Hoerr,[1] of the Crile Clinic, has in several cases inserted a soft rubber catheter into the duodenal stump and established direct external drainage. This has been a safe and simple procedure in his hands.

Obstruction of the proximal limb can be prevented by inspecting the ligament of Treitz to be certain that there is no twisting or angulation there. There should not be too much tissue turned in at the proximal jejunal opening, and twisting and angulation should be avoided. Placing the tip of a nasogastric suction tube into the proximal limb may be of some aid.

It is believed that in most instances, by careful dissection, difficult duodenal ulcers can be removed. While not entirely convinced that vagotomy with gastroenterostomy is the procedure of choice for treatment of an ulcer which cannot be removed, the authors prefer it to the exclusion operation and have used it more frequently in recent years.

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Use of Free Grafts in Correction of Recurrent Pterygia, Pseudopterygia and Symblepharon

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SUMMARY

Use of conjunctival material for grafting over areas of the eye denuded by removal of a pterygium, pseudopterygium or symblepharon gives better results cosmetically, and in some instances functionally, than either thin split skin or mucous membrane from the mouth. A technique for grafting with conjunctiva is described.

THE repair of recurrent pterygium, pseudopterygium, and symblepharon frequently necessitates the use of free graft to cover the denuded area over the sclera and into the cul-de-sacs. Usually either split skin,[8] mucous membrane,[1, 8, 10] or conjunctiva[2, 3, 4, 6, 7, 9] is used for this purpose.

Thin split skin will "take" very well, but the desquamating epithelium is very poorly tolerated by the cornea. Also, the graft becomes thicker and whiter—more unsightly—as it grows.

Mucous membrane from the mouth is available in relatively large amounts; it may be removed from either inside the lower lip or inside the cheek anterior to Stenson's duct. It shrinks moderately but grows fairly well and is tolerated by the cornea. However, it tends to remain a deep red color even with the passage of time. The thinner the graft, the less the primary contraction. It is most important to trim the graft thoroughly, allowing 10 per cent for primary contraction. The method described by Macrae[5] is an excellent one. The strip of mucous membrane, when removed, is laid across the palmar aspect of the left index finger, raw surface exposed. The ends or points of the graft can then be controlled by means of the thumb and side of the middle finger, which may be necessary when dealing with a graft which has been cut a little too thickly and thus tends to curl in. All fat and submucous tissue must be removed with fine scissors until the graft is so thin that, were it not kept on the finger during the process, it would be difficult to tell which was the raw surface. The lip wound may be sutured later; while the material is being prepared, bleeding at the donor site may be controlled by pressure.

The mucous membrane graft is transferred to the already denuded area on the globe and sutured into place with interrupted 6-0 black silk. The graft is trimmed as necessary at the time of suturing. Care must be exercised to cover areas well into the cul-de-sac. It may be necessary to use double arm 4-0 silk sutures carried from the cul-de-sacs to the outside and tied over pegs. The caruncle should be preserved if at all possible and not covered with a graft.

A plastic oval conformer with a central opening a little larger than the cornea is introduced to hold the graft well into the cul-de-sacs and allow some pressure to be placed over the graft.

In estimating the size of graft required, it is helpful to know the anatomical facts concerning the human eye. The superior conjunctival fornix corresponds nearly with the superior palpebral skin fold.[11] The conjunctival fornix lies 8 to 10 mm. from the corneal margin above and below, and 7 mm. from the internal canthus. With the eye closed the conjunctival fornix is distant from the palpebral fissure 20 to 25 mm. above and 9 to 12 mm. below.

There are few references in the literature to the use of conjunctiva.[2, 3, 4, 6, 9] Advantages of this material are that it is easy to procure in most instances, it heals into place well, and it matches the cornea better than other materials. It may be taken from either the affected or the opposite eye. The major disadvantage is the limited amount available. A technique of grafting with conjunctiva which the author has found satisfactory is as follows:

The upper lid is everted over a large-sized Desmarres retractor held on the skin surface. A 2 per cent solution of procaine with epinephrine 1:40,000 is injected with a 27-gauge needle just under the conjunctival surface 3 to 5 mm. posterior to the superior edge of the tarsus. Several small amounts are injected along the line to balloon the conjunctiva so that it resembles a long sausage. With the conjunctiva thus stretched, a strip 20 mm. long by 10 mm. wide is outlined with a sharp knife and then carefully undermined longitudinally, with the point of the scissors kept close to the conjunctiva. The ends are then cut free and a 6-0 black silk suture is placed through each corner to aid in identifying the epithelial surface, in handling the graft, and in stretching it immediately after it is transferred to the recipient area. As the conjunctiva has been stretched vertically by the previously mentioned injection, it immediately contracts about 30 per cent so that the width of 10 mm. reduces to approximately 7 mm. The graft is sutured into place, care being taken to cover the cul-de-sacs if necessary. A plastic conformer is placed in the eye. The donor area is sutured with 6-0 black silk.

Presented before the Section on Eye, Ear, Nose and Throat at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

A dressing of fluffed gauze, kept under moderate pressure with adhesive tape and a head roller bandage, is used. The dressing is changed in five days and every three days thereafter. The conformer and sutures are removed in two weeks.

The results in a small series of cases have been most favorable. There is a shortening of the upper cul-de-sac where the graft was removed but not enough to produce subjective symptoms.

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Discussion by ORWYN H. ELLIS, M.D., *Los Angeles*

Regarding skin grafts to cover sclera and repair conjunctival defects, I heartily agree with Dr. Hartman that dermal grafts are unsightly, have a copious foul-smelling mucopurulent discharge, and are rarely if ever indicated. I have made infrequent use of mucous membrane for grafting. It is almost never necessary to suture the lip or mouth wound, unless the deeper structures have been inadvertently entered.

Conjunctival grafts interest me most. In traumatic wounds or chemical burns, usually the upper fornix remains uninjured and can be ballooned as Dr. Hartman has described. Then the conjunctiva from the fornix of the same eye is swung down as a large pedicle graft or excised as a free graft to cover the defect of the bulbar conjunctiva, to line at least one side of a symblepharon or wherever it is indicated to suture in place. In this regard one point should be mentioned. It is not necessary to suture or even to try to approximate the area from which the graft, either free or pedicle, was taken—provided that only the conjunctiva was removed and the underlying tissue was not injured in taking the graft. Shortening of the cul-de-sac has not been observed if the stent remained in place three weeks. The chance of injury is greatly lessened by the subconjunctival procaine injection, which should be carried out whether the operation is to be done with general (which I prefer) or local anesthesia. The conjunctiva quickly regenerates without defect with the stent in place, and is usually fully healed without contracture in three weeks, at which time the large pressure dressing can be permanently removed.

In cases in which pterygia repeatedly recur after simple excision (which, in my opinion, has the most to offer of all the operations for pterygium) I have done a lamellar or split-thickness corneal graft with success. In such cases, this procedure, rather than repair using conjunctiva or mucous membrane, is indicated. After excision of the recurrent area from the cornea by corneal splitting, a split-thickness graft from a donor eye, cut to fit the defect in the host cornea, is applied with direct suturing. Tract sutures have been found to ease considerably the task of suturing the corneal graft in place.

Apoplexy in Young Adults—Diagnostic and Therapeutic Observations

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SUMMARY

Apoplexy in young adults is due to rupture of an artery or to obstruction, as by clot, by embolus, or by transitory vasospasm. In differential diagnosis, tumor and demyelinizing disease must be considered.

Spinal fluid study helps to differentiate between hemorrhagic stroke and stroke due to vascular block. In hemorrhagic stroke, search for the site of bleeding is imperative and angiography, the preferred method of study, should be carried out as soon as the patient's general condition permits.

In vascular occlusive stroke, measures to maintain the blood pressure and to dilate collateral channels are often helpful. Stellate block is most valuable in the acute phase immediately following embolism or thrombosis. In a small percentage of chronic cases, stellate block may be followed by significant recovery of function. Benefit may also be derived at times from systemic vasodilators such as niacin and intravenously administered histamine.

APOPLEXY, also referred to as "stroke," is the sudden diminution or paralysis of consciousness, sensation or voluntary motion resulting from the rupture or obstruction of an artery of the brain. The evidence of apoplexy may include any or all of the three objective factors either singly or in any combination.

Traditionally apoplexy has been regarded as one of the degenerative diseases affecting principally persons in the later years of life. Its occasional occurrence in young adults has been the object of intensified interest in recent years because of the development of improved modes of diagnosis and subsequent refinement of therapy. Young adults, by which is meant those persons who have not yet passed the fifth decade, may be subject to the same deteriorative diseases as are their elders. In addition, a considerable number of vasospastic diseases and embolic phenomena occur in this age group, and the likelihood of congenital anomalies, particularly saccular aneurysm and arteriovenous angioma, is greater. The general tissue reserve of young adults permits a wider range of therapeutic trial and provides a more substantial basis for objective evaluation of treatment.

The diagnosis of apoplexy in young adults, while generally simple, may on occasion be complicated. Other lesions capable of abrupt onset, such as brain tumor, or demyelinizing disease such as multiple sclerosis, may be initiated in a similar fashion. Differentiation between hemorrhagic stroke and that due to vascular blockage may also be complex, although as a rule the presence or absence of blood in the spinal fluid will permit a ready distinction between the two. The value of angiography in identifying and localizing the lesion has become widely recognized, although here, too, limitations are imposed which, if ignored, will lead to false deductions.

The immediate causes of apoplexy fall readily into two categories: Vascular occlusion, and vascular rupture. Of these, occlusion will be considered first. Vessels leading to the brain or its subdivisions may be blocked by an embolus, by vascular spasm, or by a thrombus. Any of these may occur at any time and apparently in any circumstances, although thrombus is more liable to occur in a situation where the rate of blood flow is reduced.

The diagnosis of embolism is made when, associated with apoplexy, a potential source of embolus —such as cardiovascular thrombus, dislodged fat, or air—is recognized. Postpartum stroke also is felt to belong to this category.

In certain circumstances the onset of stroke from embolism may be heralded by a convulsive seizure. Involvement of consciousness may be associated with block of a large vessel or with interruption of certain of the smaller channels. Sensorimotor function is more commonly involved on the right side of the body, representing cerebral embolism on the left side, probably because of the mechanics of the vascular supply.

Spinal fluid pressure ordinarily is not elevated following embolic stroke, and in the acute stage the cell and chemical contents of the fluid are not materially altered. The block may be followed by extravasation of blood by diapedesis and later there may be frank rupture of the vessel due to the weakening of the vascular wall, but it is unlikely that these will play any major part in verifying the diagnosis of cerebral embolism. In the late stages, also, increase in the protein content of the cerebrospinal fluid may occur, particularly if an extended area of the brain surface has been affected.

Embolic apoplexy offers one of the most favorable situations for the therapeutic use of the anes-

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Presented before the Section on Psychiatry and Neurology at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

thetization of the cervical sympathetic chain, so-called "stellate block." Many times the patient is already under direct medical care because of the situation providing the source of the embolus; hence immediate treatment is possible with the result that damage to the cortical cells is minimal. Oftentimes the initial sympathetic block is all that is necessary, and if this is carried out within the first few minutes of onset, the return of function may be dramatic. Generally the use of niacin in a dose of 100 mg., from one to three times a day for several days after the stroke, seems desirable.

Vascular spasm may be confused with cerebral embolism as the cause of apoplectic ictus. Usually this is associated with other peripheral vascular disease, particularly arterial hypertension. In the young hypertensive person the appearance of vasospastic phenomena of itself indicates a vascular lability later eliminated by the sclerosing effect of degenerative disease. The vasospastic process may mimic embolism or thrombosis; it is recognized, of course, that vascular spasm is a significant factor in embolism, thrombosis and hemorrhage. The isolated effect of spasm alone seldom produces complete occlusion; the degree of effect, therefore, is usually not as great as when other factors are involved. This state of incomplete interruption of the blood flow permits of more latitude in time than with thrombosis or embolism.

In stroke due to uncomplicated vasospasm, the cerebrospinal fluid pressure, cell count and chemical contents are at first usually within normal limits. The onset of the disease is usually not quite so abrupt as with embolus or hemorrhage. Again the patient is often already under supervision and the onset of ictus immediately brought to the attention of a physician acquainted with the medical background. When cervical sympathetic block on the ipsilateral side is carried out early there is often rapid clinical evidence of the return of cerebral function, frequently dramatically manifested. Since the underlying process in vasospasm usually persists, recurrent episodes are not uncommon.

Thrombosis of cerebral vessels again presupposes vascular disease. Thrombosis may follow embolism or vasospasm and often occurs as a delayed manifestation in hemorrhage. Atheromatous plaques may provide the basis for the accumulation of clot. Interruption of the continuity of the endothelium is thought to be essential to the development of clot. It is well recognized that slowing of the rate of blood flow is a major contributing factor. Thrombosis producing apoplectic manifestations may occur in the vessels within the cranium itself or in the internal carotid artery distal to the bifurcation of the common carotid. Thrombosis in the cervical area is not uncommon and is usually followed by strikingly diffuse manifestations which vary to some degree depending upon the amount of collateral supply from other vessels contributing to the circle of Willis. The apposition of the internal carotid artery to the lateral surface of the atlas may result in demonstrable constriction of the artery, slowing the blood flow and occasionally producing thrombus at this point. Thrombosis in the basilar artery never, and in the vertebral artery seldom, is compatible with life.

Thrombosis, when recognized as an acute problem, may be treated with some success in the manner that is suggested for embolism and vasospasm. In a considerable number of cases the problem is one of chronic paralysis, probably the result of thrombosis. Occasionally the differentiation between thrombosis and hemorrhage will be difficult in these chronic situations. In such circumstances cerebral angiography is strongly advocated. In angiographic studies, angioma and aneurysm have been encountered in some cases, and extensive thrombotic involvement of one or both internal carotid arteries also has been observed. The information thus obtained is most valuable in advising the patient as to therapy and in estimating prognosis.

The treatment of chronic effects of thrombosis produces a less satisfactory result than that which may reasonably be anticipated in the acute stage. Many of the patients have profound emotional as well as sensory and motor afflictions, the former representing extensive basal ganglion involvement. It is necessary for both physician and patient to recognize at the outset that return to completely normal function is unlikely. Interruption of the cervical sympathetic nerve by procaine has been tried. Electroencephalograms taken immediately before and after the block, and careful objective and subjective analysis of change in the sensorimotor or emotional spheres, provide the basis of evaluation. If the result of chemical nerve block seems adequate, cervical sympathectomy or stellate ganglion decentralization may be indicated. Repeated stellate block will be disappointing, for the effectiveness of the local anesthetic agent has been observed to diminish rapidly. Intravenous histamine injections, suggested by Furmanski,[1] have been of value in instances where a surgical procedure does not seem justified. The administration of 1 mg. of histamine in 250 cc. of Ringer's solution or 5 per cent dextrose solution, intravenously, at a rate sufficient to produce a flush, and repeated as often as three times a week, has been followed by significant somatic and emotional improvement.

Embolism, vasospasm and thrombosis are all secondary manifestations of some underlying disease in the body. The necessity of treating the underlying disease must, of course, always be remembered and the cerebral problem regarded in its true situation as only one aspect of a general medical problem.

Apoplexy due to hemorrhage is the other broad division of this general problem. In young adults, cerebral hemorrhage may often be the result of rupture of a congenital saccular aneurysm or the result of rupture of vessels in an arteriovenous angioma. Hemorrhage may also result from vascular tear at the site of an arteriosclerotic plaque, from arteriovenous fistula, or from degenerative change in a tumor.

Hemorrhagic stroke in young adults can occur at any time. A demonstrable association between the onset and some physical or emotional strain is not consistently observed. It is reasonable to assume that rupture of a weak spot in the vascular tree is more liable to occur when factors which elevate the blood pressure come into play. However, hemorrhage is known to have occurred while the patient was engaged in conversation, while shaving, while lying in bed, after awakening in the morning, and while indulging in many other of the normal daily activities of life not generally associated with a particular alteration in blood pressure.

The hemorrhagic aspect of an ictus is generally diagnosed by the headache progressing to pain and stiffness in the cervical spine or by the overwhelming interruption of all conscious cerebral activity. Usually it can be proved by the demonstration of blood in the cerebrospinal fluid after such an incident. It is possible, however, for intracranial bleeding to occur without immediate significant change in the cerebrospinal fluid. Spinal puncture to establish the diagnosis of brain hemorrhage is felt to be unattended by any significant increase in hazard by reason of possible dislodgement of clot.

Cranial bruit is sometimes heard following hemorrhage, and may indicate an arteriovenous fistula or arteriovenous angioma. On the other hand, hemorrhage into the cranial cavity may distort the vascular tree to such an extent that bruit may result. The presence of bruit is not consistently helpful in determining the site of hemorrhage or even the side on which it occurs. Nor can the vessel bleeding be identified consistently by observation of clinical symptoms preponderantly referable to one side or the other, for aneurysms of the circle of Willis rupturing on its medial aspect may produce their major destruction in the contralateral hemisphere. Hemorrhages from the anterior communicating artery notoriously produce clinical symptoms on either side or even symptoms that suggest a rupture in the posterior part of the head.

The immediate treatment after hemorrhagic stroke is purely supportive in an attempt to permit the brain to adjust to the sudden accumulation of intracranial blood and the clotting mechanism to stem the flow from the tear in the vessel. Indiscriminate ligation of vessels in the neck on clinical grounds alone cannot usually be defended. Bleeding of hypertensive patients to reduce the arterial pressure has theoretical advantages, although the demonstrable evidence of help from this maneuver is open to some question. Cranial decompressive procedures in the acute stage are seldom if ever of sufficient value to justify the additional strain of a surgical procedure carried out at a time of crisis.

Direct and positive approach to the treatment of the bleeding point necessarily rests entirely upon the demonstration of the location and character of the bleeding point by cranial angiography. Angiograms should be obtained as soon after hemorrhage as the patient's general condition permits. Angiography should never be attempted, however, when the patient's condition is precarious. On the other hand, there is as yet no evidence that an injection of Diodrast® or Thorotrast® into the common carotid artery through a needle up to 18 gauge in size will materially increase the pressure in that artery. No rise in pressure was noted in direct readings in a small number of cases.* Actually, in some instances there was an apparent fall in pressure which theoretically might be related to the slowing of the pulse so often attendant upon injection of Diodrast.

Angiograms may demonstrate aneurysm or angioma, or may show no abnormality. For aneurysm arising from the carotid artery itself, ligature in the neck is the preferred treatment. This is usually done under local anesthesia and is sometimes followed by intracranial trapping. A pedunculated saccular aneurysm may be clipped across the neck with a good chance of producing cure. An atheromatous plaque at the base may prevent the accomplishment of this endeavor, however, and such plaques are not demonstrable except by actual observation in the operating room.

For aneurysms distal to the bifurcation of the internal carotid artery into the anterior and middle cerebral arteries, direct approach is necessary — either ligation of the entire vessel upon which the aneurysm arises, or, preferably, if it is possible, ligation across the base of the aneurysm so that the continuity of the supplying vessel is preserved. Aneurysms of the anterior communicating artery are particularly difficult to handle because they frequently receive major supply from both anterior cerebral vessels. The interruption of both is not consistent with life. Some investigators believe that aneurysms in this region should be completely abandoned, and the patient's fate left entirely to chance. In certain instances the aneurysms definitely are not operable; on the other hand, the establishment of a fixed ruling seems unreasonably defeatist.

Arteriovenous fistula has been found to exist between the posterior cerebral artery and the vein of Galen, and between the carotid artery and the cavernous sinus. Often the contributing artery can be interrupted and when this is the internal carotid the procedure is more safely done under local anesthesia. Intracranial trapping, however, may be necessary to achieve adequate block of the fistula.

Arteriovenous angioma, a completely inoperable lesion prior to the development of cranial angiography, is now found to be operable in about 50 per cent of instances. By means of angiography the major contributing vessel can usually be demonstrated, and with experience the auxiliary contributors from the cerebral depths can be anticipated and controlled. Deep-lying angiomas involving the entire thalamus, or smaller ones which have arisen in the vicinity of the vein of Galen, have generally been avoided unless by repeated hemorrhage the excessive danger of the lesion to life becomes evi-

* The readings were taken by Dr. Lawrence Arnstein in the neurological surgery laboratory of the University of California School of Medicine.

dent. Those tumors whose vessels are at all accessible have been operated upon, the purpose being to prevent the patient's dying from massive hemorrhage. Such an end can be anticipated if the angioma is not so approached: In the author's experience a considerable proportion of patients with angiomas that were not operated upon died during the period of observation, usually within a matter of one to three years.

For the third group of patients, those who have had objective evidence of hemorrhage but in whom the arteriogram demonstrates no source of bleeding, sharp limitation of activity with absolute bed rest for at least two months and gradual return to activity approaching normal for the next two months, is recommended. Failure of demonstration of the source of bleeding has been interpreted by the author to mean that the bleeding was from a small tear, as at an atheromatous plaque, or that it was from an aneurysm which had become filled with clot between the time of hemorrhage and the time of angiography. The rationale of absolute bed rest for two months is to give adequate time for the clot to become replaced by scar tissue, which, hypothetically, will be sufficiently firm in that time to justify the gradual reestablishment of normal activity. The patient always is warned against physical or emotional strain on the hypothetical grounds mentioned earlier. This mode of treatment is an adaptation of the so-called conservative treatment which previously was recommended in all cases of cerebral hemorrhage. It has been successful in treatment of patients without demonstrable lesions. But in the author's experience it has not been successful for patients with a demonstrable lesion; in several instances the patients died, some of them during the period of prolonged bed rest.

In evaluating the results of treatment in apoplexy in young adults, it is necessary to recognize first the danger of the underlying disease process, and secondly the probable limitations of any therapeutic measure. In occlusive apoplexy the danger to life is usually greatest at the time of or immediately following the occlusion. The benefit from vasodilating mechanisms is directly proportional to the promptness with which they can be instituted and to the size and location of the vessel affected. In general, vessels mainly supplying the brain cortex react favorably to treatment by vasodilating mechanisms. If the degenerative change is in the white matter or tracts of the brain, the evidence is that no improvement can be anticipated.

In the matter of hemorrhagic apoplexy the danger to life exists until the source of bleeding is controlled or isolated from the circulation. The primary end, then, is preservation of life. A secondary consideration is the limitation of the degree of residual morbidity. Frequently saccular aneurysm, and occasionally arteriovenous angioma, may be adequately dealt with without apparent morbidity. Some morbidity is often associated with the ictus itself where the source is aneurysm, and this can usually be anticipated with angioma. Vasodilating mechanisms may minimize the morbidity from a hemorrhagic ictus to the degree that auxiliary vasospastic phenomena have affected the adjacent cortex. Much hemorrhagic damage is to the white matter, however, and here again no benefit can be anticipated.

The problem of morbidity and mortality must in some way be brought to the consideration of the patient, for in the last analysis he must make the decision. In the author's experience, most patients prefer some incapacity to a continued existence under a Damoclesian sword.

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The Surgical Treatment of Mitral Stenosis

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SUMMARY

A surgical procedure known as commissurotomy, devised by Bailey for the relief of certain cases of mitral stenosis, gives promise of considerable benefit to a large number of patients who have the disease. The technique of the operation involves the introduction of the right index finger and an especially designed valvulotome through the left auricular appendage into the left auricle. The mitral valve commissures are then divided. Twenty-five cases of mitral stenosis in which this operation was performed are discussed.

COMMISSUROTOMY is rapidly becoming the accepted surgical treatment for the relief of mitral stenosis. The procedure was devised by Bailey in 1948,[2] and subsequent reports[3,8,9,15] have given additional evidence that this procedure is beneficial to patients with mitral stenosis. In this communication data are given on 25 cases in which commissurotomy was performed.

The development of a satisfactory procedure for the surgical relief of mitral stenosis is a tremendous advance in the field of cardiovascular surgery. It is the first step toward the treatment of intracardiac deformities by direct attack upon them. Moreover, it opens the field for the further development of procedures for the relief of other acquired cardiovascular diseases. The success of the procedure attains greater significance when the prevalence of mitral stenosis is considered. It probably occurs more frequently than any other kind of valvular cardiac lesion. Bailey[2] estimated that at least one million people in this country have the deformity and that one fourth of them are candidates for surgical treatment.

The most logical approach to the problem of the relief of mitral stenosis is the prevention of rheumatic fever. Although at the present this cannot be accomplished, studies by various investigators have indicated that giving adrenocorticotropic hormone (ACTH) or related compounds during the acute stage of rheumatic fever shortens the course of the disease and may lessen or prevent residual cardiac damage.[7,12,14,21] As Bailey noted, only a minority of patients with mitral stenosis have symptoms severe enough to necessitate surgical relief. These patients have rapidly progressive symptoms of dyspnea, pulmonary edema and hemoptysis, which culminate in death. Wolff and Levine[23] stated that 66 per cent of patients who have serious hemoptysis die within three years after the onset of hemoptysis. Levine[13] also stated that the average length of time between the appearance of congestive heart failure and death is less than five years. Young women under the age of 30 make up the largest group of patients with progressive mitral stenosis and congestive heart failure.

In most patients to be considered for operation the diagnosis offers no problem. However, very early lesions might present some difficulty. It is helpful to obtain a history of rheumatic fever. Such a history can be obtained in as high as 70 per cent of patients with rheumatic heart disease. In another 5 to 10 per cent a history of chorea without rheumatism usually may be obtained. In early cases in which complaints only of increasing exertional dyspnea or easy fatigability are elicited, cardiac enlargement is not a prominent finding, although in fluoroscopic examination enlargement of the left auricle and right ventricle may be observed. If there is mitral valve obstruction of long standing, however, the heart is usually greatly enlarged. A presystolic murmur of "crescendo" type which is heard best at the apex and referred to the axilla is characteristic. A systolic murmur, which may be present in some cases, indicates mitral regurgitation. A thrill over the apical region may be associated with the diastolic murmur. Increasing fatigability and progressively increasing exertional dyspnea may be the only symptoms in some cases; in the more advanced ones, however, a history of embolic phenomena and of dyspnea, orthopnea, pulmonary edema and hemoptysis often may be obtained.

The concept of the surgical treatment of mitral stenosis is not a new one. In 1902 Sir Lauder Brunton,[5] an English physician, upon noting pronounced stenosis and calcification in the mitral valve of a patient who had died of rheumatic heart disease, concluded that surgical incision of the stenotic valve provided the only method of treating advanced mitral stenosis. It was not until 1922, however, after improvements had been made in thoracic operations and in anesthesia for thoracic operations, that mitral valvulotomy was attempted. At this time Cutler and Levine[6] excised a portion of one of the leaflets of the mitral valve in four patients. They based their procedure upon the hypothesis that the patient could withstand mitral regurgitation better than stenosis. They excised a portion of one of the leaflets to relieve the stenosis although they knew that the degree of insufficiency simultaneously would be increased.

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Aided in part by a grant-in-aid from the United States Public Health Service.

Presented before the Section on General Surgery at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

They carried out the procedure by passing a punch-like instrument through the left ventricle to engage the valve ring. Three of the four patients died in the early postoperative period, but one survived for about four and one-half years and was thought to be improved.

In 1923 Allen and Graham[1] carried out extensive investigation on laboratory animals, using a cardioscope which they passed through the left auricular appendage to visualize the interior of the heart. They had no difficulty in dividing the mitral valve in dogs, but their attempts to apply this technique to a patient with mitral stenosis resulted in death at the time of operation. The preoperative condition of this patient, however, had made surgical intervention extremely hazardous.

During the years subsequent to 1929 several isolated attempts were made to deal directly with the mitral valve. The method most used was to incise the valve ring directly as Cutler and co-workers had done. Souttar,[19] however, carried out digital dilatation with success in one case.

After these attempts interest was directed toward the development of a method for the production of mitral stenosis in experimental animals so that the operation might be advanced from a more fundamental and physiologic point of view. Powers[16] in 1929 reported a method for the production of mitral stenosis in dogs by cauterizing the valvular cusps with diathermy and injecting cultures of streptococci into the blood stream. About the same time, Wilson[22] devised another method of producing stenosis experimentally. He placed strips of pericardium across the left auricle immediately above the mitral valve so that the valve cusps would strike the bands constantly, thus becoming traumatized. The trauma produced fibrosis, which resulted in some degree of stenosis. Neither of these methods has been considered satisfactory.

Almost no work was carried out on the correction of valvular stenosis until after World War II. The revolutionary work in the surgical treatment of some of the congenital cardiovascular deformities stimulated developments in the problem of acquired valvular stenosis. Several workers, including Smithy and Parker,[17] Bailey,[2] and Harken[10, 11] investigated this problem both in the laboratory and in the operating room. In 1947 Smithy[18] recorded the results of investigation on experimental animals and also reported the outcome of valvulotomy on a series of patients. He felt, as others had previously, that valvular insufficiency was better tolerated than a stenotic lesion. Using an instrument similar to Cutler's, which he passed through the left ventricle, he punched out a circular portion of the posterior valve leaflet. He operated upon seven patients, two of whom died in the immediate postoperative period. The valve was missed in two of the remaining five. Harken initially approached the valve through the left superior pulmonary vein but subsequently employed an instrument which he passed through the left auricular appendage. Bailey initially dilated the valve with his finger but, after one such operation, incised the valve commissure with a hooked knife concealed beneath a second glove along his finger. This procedure, which removed no tissue from the valve ring, he termed "commissurotomy." The operations developed by Harken and Bailey constituted the first attempts to relieve stenosis without producing valvular insufficiency. Bailey has now operated on a large series of patients with his method. The over-all mortality rate is under 10 per cent. The patients who lived were considerably benefited.

While these valvular operations were being developed, several indirect approaches to the problem were attempted. Many physicians had noted that patients who had Lutembacher's syndrome of congenital interauricular septal defect associated with mitral stenosis had less severe clinical symptoms than patients who had mitral stenosis without the associated deformity. In an attempt to reproduce this compensatory effect, Harken created an interauricular defect in two patients with mitral stenosis. Another approach which Harken used was to interrupt the sympathetic accelerator and afferent cardiac nerves to control heart action. He used this method on several patients with severe symptoms and with rapid heart action which could not be controlled by medical measures. Still another approach, which Bland and Sweet devised[4, 20] was to shunt a portion of the pulmonary venous return back into the systemic venous system. This they accomplished by anastomosing the distal end of a branch of one of the pulmonary veins to the proximal end of the azygos vein. They used this procedure on six patients. The first three were improved. Two (at the time of report) had been operated upon too recently for satisfactory evaluation. One died after an exacerbation of acute rheumatic fever in the immediate postoperative period.

In comparing the results of all attempted treatments, the author concluded that the procedure which Bailey employs appears to offer the greatest long term benefit and has selected commissurotomy, therefore, as a routine procedure.

OPERATIVE PROCEDURE

The method used by the author follows the principles of the procedure devised by Bailey but employs a different instrument (Figure 1). This instrument has a hook on either side so that the median commissure can be divided without pronating the hand. Moreover, it is curved transversely as well as longitudinally to fit the contour of the transverse curve of the finger, a feature which obviates the need for the second glove, which is used to attach the Bailey knife to the index finger.

A maintenance dose of digitalis and doses of quinidine up to about 0.4 gm. every three to four hours are administered before operation. Penicillin, 100,000 units every six hours, is usually given three days prior to operation. Preanesthesia medication of scopolamine and morphine and an anesthetic, usually sodium pentothal and endotracheal ether, are administered.

An anterolateral incision is made through the fourth interspace. It is occasionally necessary to divide the fourth costal cartilage at its junction with the sternum. In order to gain proper exposure, the incision should be carried well into the axilla. This can be facilitated by elevating the left side of the chest and flexing the elbow in order to expose the axillary region. About 10 cc. of 4 per cent procaine solution is instilled into the pericardial cavity and allowed to remain for about four to five minutes before the pericardium is entered. A long, curved incision is then made in the pericardium in such a manner that a flap is formed, the base of which is anterior and parallel to the phrenic nerve. A purse-string suture of No. 00 silk on an atraumatic needle is placed about the auricular appendage at its junction with the chamber of the auricle. The auricle is occluded temporarily by a non-crushing clamp placed at its base, and the tip of the appendage is excised. The finger is introduced into the auricle, the clamp is removed, and the valve is palpated.

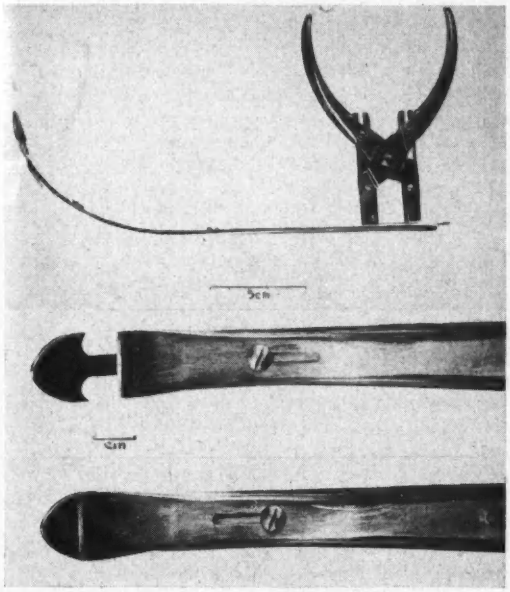

Figure 1.—Photographs of valvulotome used for mitral commissurotomy. *Top*—Lateral over-all view of valvulotome. *Center*—Open end of valvulotome with hooked knife on both sides. *Lower*—Closed valvulotome.

Occasionally an extremely stenosed valve orifice is difficult to find. A jet of blood, which sometimes may be felt passing into the auricle with each systole, is helpful in locating the valve. (Calcification of the valve was present in a high percentage of the cases.) The finger is passed into the valve opening, which is then moderately dilated. If one of the commissures tears easily, an attempt is made to continue this tear. The valvulotome is then passed into the auricle along the finger (Figures 2 and 3). The anterolateral commissure is usually divided first (Figure 4). If the opening is still too small, the median commissure is divided. The incised areas are then slightly dilated with the finger. The finger

Figure 2.—Photograph of valvulotome in position to divide the anterolateral commissure in an autopsy specimen of a heart with mitral stenosis. Most of the auricular wall has been cut away.

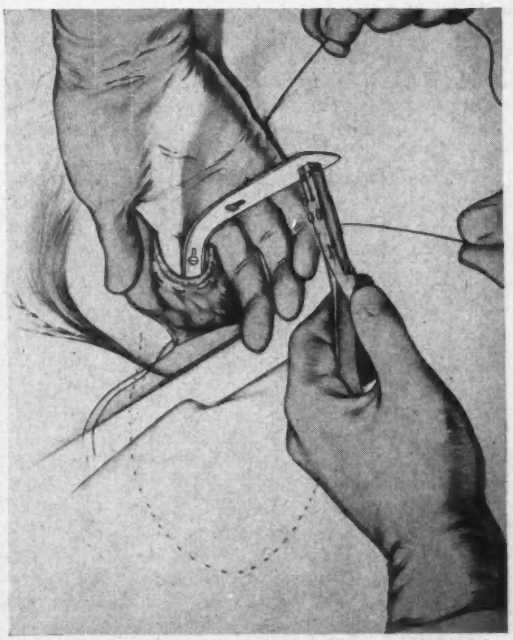

Figure 3.—Drawing of right index finger and valvulotome inserted into the left auricle through the left auricular appendage. The ends of a purse-string suture encircling the appendage are held by an assistant.

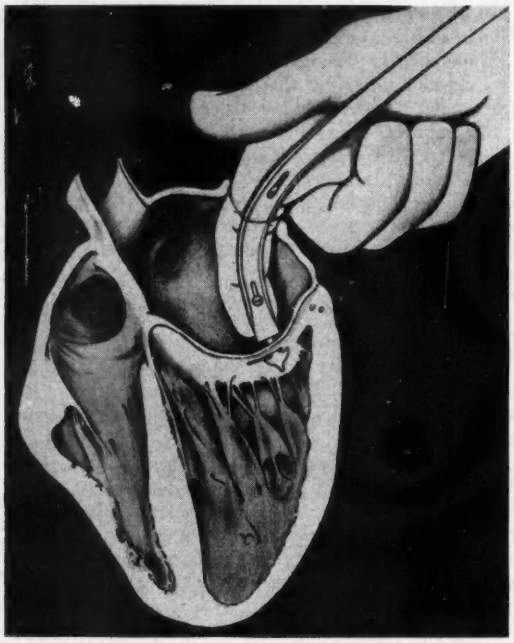

Figure 4.—Sectional view of the heart with the anterolateral commissure engaged in the open end of the valvulotome. The posteromedial commissure may be divided by moving the valvulotome to the opposite side of the valve orifice.

is withdrawn, and the purse-string suture is tied. The cut end of the auricle in most instances is oversewn with an arterial suture. The pericardium is closed loosely so that any accumulated fluid can drain into the pleural cavity. The chest is closed in layers with interrupted silk sutures, and intrapleural catheter drainage is placed.

PRESENTATION OF CASE MATERIAL

The majority of the 25 patients in the series here reported upon were in the older age group. Fourteen were over the age of 35; the oldest was 51. Four of the patients died. One of them, who at first appeared to be much improved, died three weeks after operation of a pulmonary embolus, observed at autopsy. Another died of cardiac arrest after moderate hemorrhage due to a tear in the wall of the auricle. The bleeding was controlled, but cardiac contractions could not be reinitiated. This patient was 42 years of age and had both aortic and mitral valvular lesions. The third patient, a 38-year-old male, died on the fourth postoperative day from rapidly progressive heart failure. He had had long-standing heart disease and constant heart failure with associated liver congestion, which had caused slight jaundice for some time. There were also infiltrating lesions in both lungs, the cause of which was undetermined. Valvulotomy was carried out as a last resort. Although the patient withstood the procedure well, auricular fibrillation with a high pulse rate and high pulse deficit began soon after operation, and he died on the fourth postoperative day. In the fourth case in which death occurred, cardiac arrest developed before the incision was made. The heart was immediately exposed, and cardiac contractions were reinitiated by the administration of epinephrine and cardiac massage. The anterolateral commissure was quickly divided, but the patient did not respond properly and died 18 hours after operation.

All the patients in the series had had symptoms of rheumatic heart disease for from six months to 20 years. Many of them had far advanced symptoms of pulmonary hypertension with pulmonary edema and hemoptysis. Five had auricular fibrillation before operation. Six had had peripheral emboli, and two of them had residual hemiplegia.

Of the 21 patients who survived the operation, all appear to be improved to some degree. Congestive failure occurred during the first two weeks in six cases. In three it was precipitated by a respiratory infection. Increasing the dose of digitalis and administering mercurial diuretics relieved the cardiac decompensation except in one case, previously mentioned, in which the patient died. Pulmonary edema and hemoptysis have not recurred in the surviving patients. Exertional dyspnea has diminished and exercise tolerance has increased in most cases. It is still too early to make the prognosis for the final outcome, but it would appear to be favorable.

DISCUSSION

Although patients treated by commissurotomy have been observed a relatively short time, the procedure appears to offer immense benefit to a large group of patients. The fears voiced by many during the developmental stages of commissurotomy that the incised areas would heal together now seem unfounded. Although valves which have been divided several years previously must be examined in order to determine whether stenosis recurs, the indications thus far are encouraging. The author noted no evidence of healing in the patient who died three weeks after operation, and Bailey noted no sign of reformation of the stenosis in a patient who died three months after operation. The fact that little or no additional regurgitation is produced by division of the commissures places this operation far ahead of any procedure previously devised to relieve mitral stenosis. The author and his associates have not always been able to divide the valve so that no addinal regurgitation occurs. Although great care was taken in placing the incision in the commissures, the regurgitation has increased in over 50 per cent of patients. The regurgitation can be felt by the finger in the auricle at the time of operation and can also be elicited as a systolic murmur after the procedure.

Another consideration is the possibility of occurrence of embolic phenomena after the operation. A pulmonary embolus was the cause of death of the first patient of the series, as was noted previously, and embolus was suspected in two other cases, although the presence of the lesion could not be confirmed. The author has been reluctant to employ anticoagulants because of the possibility of their causing hemorrhage.

Heart failure, either at the time of operation or in the postoperative period, is more likely to occur if auricular fibrillation is present. In an attempt to alleviate this complication, patients who are to undergo the operative procedure are given a maintenance dose of digitalis and as much as 0.4 gm. of quinidine every three hours. If auricular fibrillation exists before operation, even though it may have been present for many years, an attempt is made to convert the rhythm to normal.

Four per cent procaine solution is used in the pericardial cavity at the time of operation to prevent arrhythmias, and procaine amide is used if necessary to restore normal rhythm should any irregularity appear during the operative procedure.

Criteria for the selection of patients to undergo operation for mitral stenosis have thus far been poorly defined. Young patients with minimal symptoms only of increasing exertional dyspnea and easy fatigability tolerate the procedure the best and logically can expect the best prognosis. However, at present it is felt that older patients with advanced symptoms of pulmonary hypertension such as pulmonary edema and hemoptysis are considerably benefited by the operation. As was pointed out previously, more than half the patients in this series were over 35 and most of them improved after commissurotomy. Aortic insufficiency was not considered as contraindicative to operation unless peripheral signs were present. Several of the patients had what was thought to be mild to moderate aortic insufficiency. This diagnosis must be made with caution in the absence of peripheral signs, because a murmur characteristic of this deformity may easily be confused with a Graham-Steell murmur.

Obvious contraindications for operation are active rheumatic carditis, recent large emboli, predominant mitral insufficiency, and subacute bacterial endocarditis.

Although considerable time must elapse before the ultimate long term results of this procedure can be determined, results thus far are favorable enough to encourage its continued use in patients with mitral stenosis who have advanced pulmonary hypertension.

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Diphtheria: The Present-Day Problem

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SUMMARY

The importance of diphtheria today is made evident not only by the continued frequency of its occurrence but also by its tendency to attack the older adult population. The high mortality and complication rate can be attributed in part to this shift in age incidence, as well as to delayed recognition and treatment.

THE consideration of diphtheria as a problem in this age of preventive medicine and chemotherapy may seem at first to be unusual. However, this disease not only continues to occur with significant frequency but has become more common in recent years, most particularly in the older age groups where the mortality and complications are increasingly important. The concept that diphtheria is a disease of younger children was well established in the early part of the twentieth century, when over 80 per cent of the cases occurred in children under five years of age.[5] Even as recently as 1947, it was said that about one-half the cases of diphtheria occur in children under the age of five years.[7]

A shift in the incidence of the disease toward the older age groups was stressed by Geiger in 1945.[4] This study showed an increasing mortality rate per 100 cases based upon experience with the disease in San Francisco. The increasing incidence of the disease in the older age groups has also been noted in many other cities in the United States.[6]

The present study was undertaken to determine the recent epidemiological phenomena of diphtheria in San Francisco and to analyze the cases from a clinical viewpoint in an effort to demonstrate some of the factors influencing the recognition and course of the disease in the individual patient.

MATERIALS AND METHODS

The present investigation covers the nine-year period from January 1942 through December 1950. Statistical material on reported cases of diphtheria in the state of California and in San Francisco county over that period was made available by the State of California Department of Public Health, Bureau of Communicable Disease Control, I. M. Stevens, morbidity statistician.

The patients included in the investigation were all hospitalized in the isolation division of the San Francisco Hospital during the years 1942 to 1950, inclusive. The criteria for inclusion required that the clinical diagnosis of diphtheria had been confirmed either by the isolation of Corynebacterium diphtheriae or, in a few instances, by the occurrence of neurological complication ascribable to the toxin of this organism. The postmortem observation of pathological changes typical of the acute disease process in the respiratory tract was also considered adequate evidence. These criteria account for a great part of the discrepancy between the number of cases reported for the county of San Francisco and the number presented in this study. For example, diphtheria might have been diagnosed on clinical grounds, diphtheria antitoxin used in treatment, and the case reported to the Department of Public Health as a case of diphtheria; yet if all cultures were subsequently reported negative for Corynebacterium diphtheriae, the case would be excluded from this study.

All culture material was immediately inoculated onto Loeffler medium and placed in a bacteriological incubator. Interpretation of the cultures was carried out in the laboratories of the department of public health of the City and County of San Francisco.

The criteria for the diagnosis of the various complications of diphtheria require special note. The presence of myocarditis was confirmed in every instance, either by electrocardiogram or postmortem examination. The criteria of electrocardiographic abnormality have been described in detail elsewhere.[3]

The diagnosis of neurological complications was based entirely on the clinical observation of sensory or motor changes in the areas served by the nerve groups involved.

Respiratory obstruction was considered, for statistical purposes, to exist in those cases in which tracheotomy was done or in which atelectasis was noted either clinically or postmortem. Minor degrees of respiratory obstruction associated with laryngeal diphtheria were classified in the present study merely as laryngeal involvement.

Antitoxin was given intravenously in almost all cases.

RESULTS

Epidemiological Observations

It will be noted in Table 1 that in the state of California as a whole the incidence of diphtheria declined in the years 1948, 1949, and 1950, while in San Francisco County it increased, and the proportion of cases in California which occurred in San Francisco County increased sharply. While not every patient with diphtheria in the county was hos-

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Presented before the Section on General Medicine at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

TABLE 1.—*Total Number of Cases of Diphtheria in California, in San Francisco County, and in San Francisco Hospital*

	1942	1943	1944	1945	1946	1947	1948	1949	1950
Total Cases in California	883	1,167	1,215	1,299	1,186	774	444	457	268
Total Cases in San Francisco County	29	41	20	54	53	45	92	82	48
Total Cases in San Francisco Hospital	20	22	6	28	32	44	56	43	22
Per cent of State Cases in San Francisco County	3.2	3.5	1.6	4.1	4.4	5.8	20.7	17.9	17.9

TABLE 2.—*Diphtheria Cases in California, 1942-1950, by Age Groups*

Year	0 - 14 Years		15 - 39 Years		40 Years and Older	
	Number	Per Cent of Total	Number	Per Cent of Total	Number	Per Cent of Total
1942	525	60.6%	222	25.6%	120	13.8%
1943	785	68.5	244	21.3	117	10.2
1944	830	70.0	268	22.6	88	7.4
1945	860	67.2	328	25.6	93	7.2
1946	776	67.0	288	24.9	94	8.1
1947	467	61.6	211	27.9	80	10.5
1948	209	48.0	126	29.0	100	23.0
1949	191	42.6	160	35.6	98	21.8
1950	107	40.4	87	33.0	70	26.6

Note: Only those cases in which the age was stated are included in this table.

pitalized at the San Francisco Hospital, the difference between the number of reported cases for the county and the number of patients recorded in Table 1 as having been in the San Francisco Hospital with diphtheria is accounted for, largely, by the criteria established for inclusion of cases in the present study.

Of the total of 273 patients (San Francisco Hospital, 1942-1950) included in the study 65 per cent were males and 35 per cent females. This ratio did not vary significantly when computed year by year. The mortality rate for males over the nine-year period was 20.2 per cent and for females 17.8 per cent. In the total group of 273 cases, there were only eight Negroes and three Orientals, distributed at random over the nine-year period.

Data on cases of diphtheria in California, arranged according to the age of the patient, are presented in Table 2. Only those cases in which the age was given in the report to the California State Department of Public Health are included. There was a significant increase in the incidence of diphtheria in the group of persons aged 40 years and older, and a steady decline through the nine-year period in the incidence of the disease in the youngest age group comprising children from birth to 14 years of age. In the age group 15 to 39 years there was only a slight increase over the course of the nine-year period. In a similar analysis of diphtheria cases in San Francisco County, data were included to cover a longer span of time (Table 3) and the increasing incidence of diphtheria in the older age groups was even more striking.

In the present series of 273 cases, eight patients

TABLE 3.—*Increasing Incidence of Diphtheria in Patients Over 30 Years of Age in San Francisco*

Year	Per Cent of Total Cases	Year	Per Cent of Total Cases
1922	9	1944	35
1924	8	1946	57
1926	8	1948	69
1942	52	1950	54

Data for years 1922-1926 from J. C. Geiger, M.D., Bulletin, San Francisco Department of Public Health, October 27, 1947; for years 1942-1950 from California State Department of Public Health, Bureau of Disease Control.

gave a history of having had diphtheria previously. One of them, who gave a history of diphtheria as a child, had two separate attacks of typical diphtheritic pharyngitis in the course of a year during the present study.

In the last year of the study the Schick test was performed in a number of patients on admission one hour before antitoxin was administered. The rapid local fixation of the toxin of Corynebacterium diphtheriae makes such testing possible, and the results are little influenced by the subsequent introduction of antitoxin.[8] In 13 such tests on patients included in this investigation, the result was positive in ten cases and negative in three.

An attempt was made to determine the magnitude of the burden placed upon the hospital by cases of diphtheria. The average period of hospitalization for the patients who died was fairly constant at about ten days for the nine-year period; for patients who recovered, it ranged between 25 and 48 hospital days, with a tendency in recent years to longer

hospitalization. The total hospital time for patients who recovered averaged 1,063 days per year over the nine-year period.

CLINICAL FEATURES OF DIPHTHERIA

Location of Infection

Diphtheria may involve any part of the respiratory tract, other mucous membranes, or the skin. All but one patient in this series had diphtheritic infection of the respiratory tract (Table 4). One patient had cutaneous infection as the only manifestation and nine others had skin involvement in addition to a lesion of the respiratory system. Of the 273 patients, 173 (63.4 per cent) had a diphtheritic lesion limited to one anatomical area; 100 (36.6 per cent) had lesions in more than one area. While laryngeal diphtheria was present in 75 patients, only 12 had lesions of the larynx in the absence of pharyngeal diphtheria. In 94.1 per cent of all patients, pharyngeal diphtheria was present.

Symptoms and Signs

The systemic symptoms of early diphtheria were generally mild and insidious in onset. Soreness of the throat was rarely severe at the beginning, but increased gradually to a maximum after several days and often persisted for many days. Headache, muscular aching, malaise, and prostration were not usually severe in the early stages of infection. Fever was often low-grade or absent. Chilliness was noted frequently, but frank chills were uncommon.

The local lesion in the pharynx in its typical form consisted of a grayish, tenacious pseudomembrane, confluent over areas involved, and often extending beyond the tonsillar fossa to the posterior pharyngeal wall. Extension to the soft palate and uvula was frequently observed. Early pseudomembranes appeared translucent and merged almost imperceptibly into the surrounding mucous membrane. Later lesions appeared denser and became more sharply demarcated. Edema of the tissues was often prominent. Erythema was commonly limited to a narrow area around the pseudomembrane. Atypical lesions were common and included follicular or patchy pseudomembranes, pseudomembranes variously colored from greenish to black, complete absence of pseudomembrane, and diffuse erythema of mucous membranes.

The manifestations of laryngeal diphtheria were similar to those of other forms of laryngitis. Croupy cough, hoarseness, stridor, and obstructive dyspnea were usually present. Complete aphonia was common. When laryngeal diphtheria was suspected and there was no pharyngeal involvement, visualization of the larynx was carried out to confirm the diagnosis.

Anterior nasal diphtheria was characterized by persistent nasal discharge, often blood-tinged and frequently unilateral. Pseudomembrane was usually visible after removal of secretions.

Cutaneous diphtheria was observed as an ulcerative lesion which did not necessarily have pathognomonic features. Early lesions often consisted of flat bullae partly filled with pus, surrounded by an area of erythema. Late ulcers were only occasionally covered by pseudomembrane and were clinically indistinguishable from other indolent ulcers. Anesthesia of the base of the ulcer occurred in several patients. This symptom was of great diagnostic aid.

Complications

Myocarditis, obstruction of the respiratory tract, and neuritis were the most commonly noted complications of diphtheria (Table 5). Myocarditis and neuritis occurred more frequently in the older age groups, while respiratory obstruction was more common in children. In addition, pneumonia occurred in five patients, nephritis in five, embolism of the femoral artery in one, and general hemorrhagic tendency in one.

Myocarditis occurred in 100 patients (36.6 per cent). The average time of appearance after the onset of infection was 9.8 days; the range was from two to 47 days. It appeared on the average earlier (7.2 days) in patients who died than in those who recovered (11.4 days). In many instances of myocarditis of mild degree, electrocardiographic abnormalities were the only manifestation. In more severe cases anginal pain, abdominal pain, syncope, pallor, vomiting, hypotension, arrhythmia of many varieties, deterioration in quality of the apical first heart sound, gallop rhythm, and murmur were noted. Abnormalities as observed electrocardiographically often lasted weeks or months but appeared to be permanent in only one patient. Of 100 patients in whom myocarditis was diagnosed, 36 died.

Severe obstruction of the respiratory tract occurred only in patients who had involvement of the larynx, sometimes in association with diphtheria of the trachea and bronchi. Of 40 patients with severe degrees of obstruction, 26 (65 per cent) died. Atelectasis and pneumonia were also considered to be of obstructive origin.

Neuritis was diagnosed in 44 patients, of whom six (13.6 per cent) died (Table 6). In 16 patients,

TABLE 4.—*Mortality Rates Related to Location of Diphtheritic Lesion*

Location	Total Cases	Deaths	Per Cent Mortality	
N	2	0	0.0	Single Location 5.7
P	158	8	5.0	
L	12	2	16.7	
C	1	0	0.0	
NP	29	5	17.2	Multiple Location 42.0
PL	43	23	53.5	
LT	1	1	100.0	
PC	7	1	14.3	
NPL	13	6	46.2	
PLT	2	2	100.0	
NPC	1	0	0.0	
NPLT	3	3	100.0	
NPLC	1	1	100.0	
	273	52	19.1	

Legend: N—Nasal
P—Pharyngeal
L—Laryngeal
C—Cutaneous
T—Tracheobronchial

TABLE 5.—*Incidence of Complications and Deaths Due to Diphtheria According to Age*

Age Group	Number of Patients	Patients with Complications	Total Complications	Patients with Myocarditis	Patients with Obstruction	Patients with Neuritis	Patients with other Complications	Deaths
0 - 14 Years	85 (31.1%)	36 (42.4%)	44	20 (23.5%)	20 (23.5%)	2 (2.4%)	2 (2.4%)	15 (17.5%)
15 - 39 Years	65 (23.8%)	28 (43.1%)	35	20 (30.8%)	5 (7.7%)	8 (9.6%)	2 (3.0%)	5 (7.7%)
40+ Years	123 (54.9%)	77 (62.6%)	116	60 (48.8%)	17 (13.8%)	33 (26.8%)	6 (7.2%)	33 (26.8%)
All Ages	273 (100.0%)	141 (51.6%)	195	100 (36.6%)	42 (15.8%)	43 (15.8%)	10 (3.7%)	53 (19.4%)

Percentages indicate incidence in age group.

cranial nerves as well as nerves of the extremities were involved. Twelve patients had neuritis only in the extremities. Four had glossopharyngeal neuritis only, and in two patients the vagus alone was involved. In ten patients who did not have neuritis of the extremities, the ninth and tenth cranial nerves were both involved. Of the six patients with neuritis who died, four had involvement of the vagus nerve. Intercostal and diaphragmatic paralysis was present in the other two. In cases in which glossopharyngeal paralysis occurred, a nasal quality to the voice and regurgitation of fluids through the nose often preceded visible diminution of palatal movement. Vagal involvement was manifested by dysphagia, accumulation of secretions, and aphonia. Neuritis of the extremities was often heralded by paresthesias and numbness, followed by diminution of deep reflexes and loss of motor power in a symmetrical fashion. An increase in the spinal fluid protein content, without pleocytosis, was common. Recovery from postdiphtheritic neuritis was often very slow but was always complete.

Glomerulonephritis was diagnosed in five patients, four of whom died. In the patient who lived, chronic glomerulonephritis with hypertension persisted. It was not certain that this lesion was diphtheritic in origin. Embolism of the femoral artery was observed in one patient and was presumed to result from a mural thrombus complicating diphtheritic myocarditis.

Treatment and Results

With rare exceptions diphtheria antitoxin was administered within a few hours after the patient was admitted to the hospital. Skin and conjunctival tests for sensitivity to horse serum were invariably performed. Antitoxin was administered intravenously, usually diluted in an infusion of 5 per cent glucose solution or normal saline solution, to all but a few patients. Those patients who had positive reaction to sensitivity tests received all or part of the antitoxin intramuscularly. Intramuscular injection was also used in a few cases in which the disease was mild and in an early stage. The dose of antitoxin ranged from 10,000 to 100,000 units; the most frequently used was 40,000 units. The size of dose depended upon the location of the lesion, whether one or more anatomical areas were involved, and the duration of the disease. The weight of the patient was given little consideration in determining the amount, and the entire dose of antitoxin was given at one time. Serum reactions occurred in 28 patients (10.5 per cent). They occurred as early as the day of treatment and as late as the 26th day after treatment; the average was 8.8 days after antitoxin was administered. Reaction was not fatal in any case.

In the latter years of the period covered by this study, most patients received penicillin intramuscularly for one week or more. In no instance did penicillin appear to affect the course of the diphtheria or the incidence of complications. As was previously reported,[2] however, there was earlier disappearance of Corynebacterium diphtheriae from the respiratory tract in those cases in which penicillin was given.

Tracheotomy for the relief of respiratory obstruction was done in 22 cases. Ten of the patients died. Suction frequently was used for relief of obstruction, and oxygen was administered when it was deemed necessary. Myocarditis was treated by complete rest, and, if associated with clinical manifestations, by oxygen and sedation. Hypertonic glucose solutions appeared to have little effect. Patients with severe hypotension were given ephedrine and infusions of plasma. Digitalis was used only in those cases in which myocarditis was associated with auricular fibrillation or flutter with rapid ventricular rate.

All patients were maintained at bed rest for three weeks or until electrocardiographic tracings became normal. Activity was thereafter gradually increased until the patient was able to care for himself at home.

The longer the time between the onset of illness and the administration of antitoxin, the greater the incidence of complications and the higher the mortality rate (Table 7). In the cases in which no com-

TABLE 6.—*Incidence and Time of Onset of Post-Diphtheritic Neuritis*

Nerve	Patients	Interval Between Onset of Diphtheria and Onset of Neuritis — Average (in days)	Interval Between Onset of Diphtheria and Onset of Neuritis — Range (in days)
Extremities	28	48.0	21-91
Ninth cranial	21	31.9	6-53
Tenth cranial	22	33.9	10-62
Other cranial	4	—	12-60

TABLE 7.—*Mortality Rate in Relation to Interval Between Onset of Disease and Injection of Antitoxin*

Day Treatment Started	No. of Cases	No. of Fatal Cases	Mortality Rate (per cent)
1	9	0	0.0
2	26	1	4.0
3	31	5	16.1
4	46	8	17.6
5	40	8	20.0
6	28	6	21.4
After 6 days	67	20	29.9

plications developed, the average duration of illness before treatment was 4.4 days. For patients who had complications and recovered, the interval between onset and injection of antitoxin averaged 5.7 days; for those who died, 6.6 days. Twenty-five per cent of patients in this series did not receive antitoxin until seven or more days after onset of disease.

In the group of cases in which diphtheria was localized to one anatomical area the mortality rate was 5.7 per cent; in the group in which lesions involved two or more areas, it was 37 per cent (Table 7). The mortality rate was highest in the oldest age group and lowest in the middle age group (Table 5). The deaths among children were largely attributable to respiratory obstruction, which was of relatively high incidence in this age group. In the cases in which the patients had obstruction and recovered, the average interval between onset of disease and injection of antitoxin was 3.4 days; in the cases in which patients died of obstruction it was 6.8 days.

DISCUSSION

It is evident from the data presented that the incidence of diphtheria, while it has decreased in recent years in the state as a whole, is still significant and warrants the continued attention of physicians.

Although the data in this report indicate that in recent years an increasing proportion of the total number of cases in the state occurred in San Francisco County, this may be in some measure misleading. While the reported relative increase in San Francisco cannot be ascribed to shifts in concentration of population (for the population of San Francisco grew considerably less rapidly in the last ten years than did that of the state as a whole), it is conceivable that there was greater frequency of recognition of diphtheria in San Francisco than elsewhere in the state, rather than concentration of occurrence of the disease there.

The traditional statement that diphtheria has no predilection for persons of any one race[5] is not borne out in the present study. The number of cases of the disease in Negro and Oriental patients was low in relation to the proportion of persons of those races in the total population of the county. Of the patients in the present series, 2.9 per cent were Negroes and 1.1 per cent were Chinese, whereas almost 7 per cent of the residents of the county are Negroes and about 2.5 per cent are Chinese. Likewise, the larger proportion of males with the disease seems of interest and is not readily explained. The relative increase in incidence in adults, and especially in adults over 40 years of age, seems most important. The explanation for this probably is that in the widespread immunization programs, the younger persons are protected while the older persons are not. Most adults have not been artificially immunized, and it is probable that development of natural immunity has decreased in recent years because of less exposure to the organism. In Schick-testing of elderly adults a high rate of susceptibility was noted.[1] The administration of toxoids to adults entails increased risk of serious reaction, unless special techniques and precautions are used.[1] The increased incidence of complications in the older age groups may explain the increase in average length of hospital stay observed in the present study. The higher mortality rate from the disease in older persons puts further stress on the importance of the relative increase in incidence in the higher age groups.

The present investigation demonstrated that clinical infection with Corynebacterium diphtheriae is not necessarily a good stimulus to the production of active immunity and that recurrence is possible. This would seem to indicate Schick testing for convalescent patients and the giving of toxoid if there is positive reaction to the test.

It is apparent that the prolonged stay in the hospital requisite for patients with diphtheria represents a real burden on the hospital facilities of a community. More widespread utilization of the relatively simple means of prevention of the disease would offer an answer to this purely socio-economic feature of diphtheria.

The outcome of diphtheritic infection depends primarily on the amount of toxin fixed in the tissues. This, in turn, depends on the location of the lesion, extent of involvement, duration of infection before antitoxin is given, and resistance of the patient. Since diphtheria toxin is fixed in the tissues so rapidly and firmly that only a small part can be neutralized by antitoxin, it is vital that unfixed toxin be neutralized at the earliest possible moment by the introduction of antitoxin. This necessitates early diagnosis and treatment based on suspicion. Since diphtheria involves the pharynx in 95 per cent of patients, recognition of the lesion in this readily visible area will permit presumptive diagnosis in almost all cases. Because the incidence of fatalities and complications rises sharply with each day of delay, antitoxin must be administered at once in all cases in which diphtheria cannot be excluded by careful examination of the upper respiratory tract. Bacteriological diagnosis before treatment is a luxury that carries with it the risk of fatal delay, although confirmation of the diagnosis by culture must be sought in all cases.

Atypical features of the disease are common and must be kept constantly in mind. Although laryngeal diphtheria is usually associated with pharyn-

geal diphtheria, laryngoscopy should be carried out in all cases of laryngitis in which diphtheria cannot readily be excluded. Nasal and cutaneous diphtheria may persist for weeks or months. Absorption of toxin is relatively slight in such cases but may result eventually in myocarditis or neuritis. Cultures should be made in all cases in which persistent nasal discharge or indolent skin ulcers are present, and treatment should be started as soon as possible if Corynebacterium diphtheriae is present.

Complications are the cause of death from diphtheria. Myocarditis and respiratory obstruction commonly coexist, and death results from their additive effect. The earlier the appearance of myocarditis, the greater the probability the patient will die. Neuritis of the tenth cranial nerve may cause atelectasis and pneumonia due to aspiration of secretions, and these complications must be dealt with by frequent suction of the respiratory tract and lowering of the patient's head. Often it is necessary to feed the patient by tube or intravenously. If there is paralysis of the muscles of respiration, a mechanical respirator must be used.

Diphtheria antitoxin is the single important agent in the treatment of this disease. Because of the necessity for immediate neutralization of circulating toxin, the intravenous route appears to be the one of choice in most instances. Exact dosage requirements cannot be stated. They vary between 20,000 and 100,000 units, depending upon the site, the extent and the duration of infection. The entire amount should be given at one time. Under-dosage and repeated small doses are to be condemned. Serious serum reactions are rare, although serum sickness constitutes an annoying problem.

Penicillin therapy, in conjunction with antitoxin, contributes little to the successful outcome of a case of diphtheria.[2] Furthermore, the administration of penicillin in no way modifies the requirement for antitoxin.

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Treatment of Closed Head Injuries

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SUMMARY

Cerebral concussion is a physiological disturbance in the brain that follows a blow on the head. The cardinal symptom is a disturbance in consciousness varying from a complete loss of consciousness to a dazed state. The phenomenon is self-limited and completely reversible.

In cerebral contusion there is actual injury to the brain. The symptoms that result vary according to the amount and location of the damage. A very small amount of damage in certain areas of the brain may be fatal, while extensive damage in other areas will be survived.

Even when a patient is unconscious after a head injury, certain simple neurologic tests can be done to determine with some accuracy the extent and location of brain damage. When the patient regains consciousness, further bedside tests can be carried out to increase the accuracy of diagnosis.

Careful observation of the patient at frequent intervals is necessary to judicious application of appropriate treatment. The physician must be on the alert constantly for signs of intracranial hemorrhage and should be ready to intervene surgically if necessary.

In most cases of injury to the head, treatment consists of supplying to the patient elements that are necessary to maintain physiologic conditions and of combating disorders arising from specific injuries to the brain.

FORTUNATELY, in the care of patients who have so-called closed head injuries—the term is applied to any injury of the head in which there is neither penetrating wound of the skull nor compound or depressed fracture—surgical intervention is seldom required, although it should always be anticipated.

The most common of injuries to the head is cerebral concussion. This condition is simply a disturbance in the normal state of the brain caused by a blow on the head that is not severe enough to cause structural damage in the brain. The disturbance is self-limited and the patient needs no more than supportive measures. In this state, there is always some disturbance in consciousness that may vary from total unconsciousness lasting from minutes to several hours, to a transient clouding of the sensorium frequently termed a "dazed" or "punchy" state. Frequently the condition is associated with more or less shock.

A more serious but less frequent kind of head injury may be classified as brain contusion. Injury of this kind may or may not be associated with fractures of the vault or base of the skull. The outcome, barring certain complications, depends largely upon the amount and location of actual damage to the brain. A relatively small hemorrhage in the pons, for instance, may cause death quickly, while a very extensive contusion of a cerebral hemisphere may be followed by recovery.

The cardinal factors of interest to the physician are the kind and extent of the injury, and the proper treatment.

Proper clinical evaluation of the condition of the patient is of utmost importance in order to determine the kind and extent of brain injury, and for this there are several simple guides.

First, it is important to know how the patient was injured. If the injury occurred as the result of a blow to the head while the head was stationary—as might happen if the patient were struck by a blackjack or a baseball—the damage to the brain is likely to be fairly well localized to the zone of impact. On the other hand, if the head was moving rapidly and struck a solid object, extensive and diffuse brain damage is more probable.

The state of consciousness following an injury is extremely important to evaluate. Since it has been shown that a persistent loss of consciousness is due to minute lesions in the hypothalamus located near the center of the brain, it is apparent that deep and prolonged stupor is indicative of severe and extensive brain injury. In most instances, the loss of consciousness occurs at the time of injury and persists for varying periods afterward. Concussion is followed by loss of consciousness that may be very transient and followed by a period of confusion and disorientation persisting for several hours. If stupor has not begun to diminish two or three hours after injury, it is probable that cerebral concussion has been complicated by actual brain contusion. Each day that stupor or coma continues decreases the chance of recovery, although patients have survived even after as long as three months of unconsciousness. The disturbance in sensorium is frequently accompanied by amnesia which may persist for several days after the return to consciousness. Retrograde amnesia also is a frequent phenomenon; the patient may have no recollection of things that happened several hours before injury.

In some instances there may be a period of lucidity following a blow on the head which may or may not have caused immediate loss of consciousness, and then a lapse into deepening stupor. In an adult this usually indicates intracranial hemorrhage and is very serious. The phenomenon is much more com-

Presented before the Section on General Practice at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

mon in children, and generally a less serious sign, although here, too, bleeding must be suspected. If bleeding occurs the patient's condition will deteriorate and neurologic symptoms referable to the area affected by it will develop. Bleeding must be controlled promptly by surgical means. If stupor following an interval of lucidity is due to localized or generalized post-concussion cerebral edema, localizing signs are not prominent, the stupor is not deep and the patient's condition begins to improve in a relatively short time.

The temperature, pulse rate, respiration rate and blood pressure, in themselves, are generally unreliable as indices of the condition of the patient. This is particularly true of children, who may have a very rapid pulse and respiratory rate in the presence of increasing stupor and progressively prominent localizing neurologic signs. An adult patient with increasing intracranial pressure will have a slowing of the pulse and of the respiratory rate while the pulse pressure tends to increase, and at the same time there will be increasing headache, nausea, vomiting and progressively deepening stupor. If there is rapidly increasing temperature in the presence of other evidences of a severe head injury, the prognosis is generally very poor. In general it is a fallacy to judge the condition of the patient on the basis of the pulse rate, respiration rate and blood pressure alone.

In conjunction with the observation of the general signs already noted, it is important to consider the presence of localized brain damage. A limited neurologic examination of an unconscious patient can be done in a very few minutes. The head should be palpated carefully and x-ray films taken if necessary to determine whether or not depressed skull fracture is present. Frequently, the skull can be seen or palpated through a scalp laceration. If a depressed skull fracture is present, special attention is, of course, necessary. The pupils of the eyes must be examined and the reaction to light observed. If one pupil is static, ipsilateral brain compression or contusion must be suspected. If both pupils are dilated and do not respond to light, it is probable that there is bilateral and extensive brain damage, and the prognosis is generally very poor. Although the extraocular muscle function cannot always be determined with accuracy, a fair appraisal can be made by careful observation of the roving motions of the eyes in all directions. If the third, fourth or sixth cranial nerve has been damaged on either side, the limitation of motion of the eyeball is evident. If there is a fixed conjugate deviation of the eyes to one side, localized cortical damage must be suspected. Examination of the ear canals should be carried out. Bleeding through a ruptured ear drum is indicative of basal skull fracture in the middle fossa. If there is discharge of blood from the nose, the source of bleeding should be determined, if possible, since nasal hemorrhage without evidence of injury to the nose usually occurs as a result of a basal fracture through the floor of the anterior fossa of the skull.

Facial asymmetry, if present, is usually evident as an unconscious patient becomes restless. If the stupor is deep, firm supraorbital pressure is frequently a stimulus painful enough to cause the patient to move the muscles of expression on one or both sides of the face. Supraorbital pressure is also a useful test in determining the relative depth of the stupor. Subarachnoid hemorrhage may occur without causing any indication of meningeal irritation for a number of hours after an injury has occurred. However, in almost all such cases there will be some stiffness of the neck after 12 hours. Also there may be positive reaction to Kernig's test, but in general this test is a little less reliable than a determination of the stiffness of the neck.

A few minutes of observation of a patient who is restless will serve to determine whether or not both sides of the body are being used with equal frequency and equal force. If motions on one side are less frequent, one must suspect local brain contusion and be alert to detect progressive paralysis of the side that is used least frequently. The withdrawal response to painful stimuli, such as plantar stimulation or deep pressure over the nail bed, also helps in determining the relative strength on the two sides. The tone of the extremities should also be noted to determine if there is any difference in tone on the two sides of the body. It is just as important to observe differences in flaccidity between one side and the other as it is to note greater rigidity. The deep and superficial reflexes should be evaluated carefully and the activity on one side compared with that on the other. Ankle clonus can be easily tested and the sole of the foot should be stroked to determine whether or not Babinski reflexes are present. Usually by carrying out these simple tests, it is possible to determine whether or not any brain damage has occurred and, if so, whether the damage is bilateral or unilateral. At times, one can go a step further and determine whether or not the damage is chiefly in the anterior, the central or the posterior area of the cerebral hemisphere.

If the patient is conscious, a more thorough neurological examination can be done. The various special senses can be tested, including the visual fields. This can be done easily with a so-called confrontation test. The test is carried out in a very few minutes by checking one eye at a time and having the patient fix his gaze on the examiner's forehead or nose. The examiner can then bring either his finger or some other small, easily seen object in from the periphery of the four quadrants of the visual fields. By this test the size, shape and location of visual defect can be determined. When the extraocular muscle functions are examined, the patient should be instructed to keep his gaze fixed on the examiner's finger, which then is moved from side to side and up and down. The failure of either eye to follow is readily apparent and at the same time the presence of nystagmus can also be observed. The corneal reflexes are simply tested by a sharp, short puff of breath directed against each cornea.

Forced and emotional movements of the face should be observed for symmetry and each side of the face should be tested for sensory acuity. The response to pin-prick will generally indicate areas of sensory impairment.

Hearing, of course, can be easily tested, preferably with a tuning fork. It is important to examine hearing as early as possible after the injury, for several reasons. Occasionally, a person with a basal fracture of the skull will have loss of hearing without bleeding from the affected ear canal simply because the ear drum has not ruptured and the blood accumulates in the middle ear. (Also, in industrial and liability cases, hearing sometimes suddenly disappears in one ear shortly after legal proceedings are instituted.) The mouth and throat should be inspected and any asymmetry in the tongue or palate noted.

Careful appraisal of the patient's speech is important. Even though the patient may be confused and irrational, various types of aphasia may be detected. Sometimes complete motor aphasia or nominal aphasia is falsely attributed to some degree of stupor or to psychic disturbance. A simple test for nominal aphasia is to ask the patient to identify a watch, a fountain pen or a box of matches.

A test of the sensory facilities should be done as soon as possible after the patient regains consciousness. Total anesthesia of one or more extremities does not occur as the result of brain damage. Frequently, however, there may be loss of one or more of the special types of sensation. For example, the stereognostic sense may be completely lost in one hand while other kinds of sensation are preserved. The stereognostic sense is tested by asking the patient to identify, without looking, a common object placed in his hand. If the stereognostic sense is disturbed, there is frequently also some disturbance in position sense. Varying degrees of disturbance in tactile sensibility, as evidenced by reaction to light touch or pin-prick on the face, trunk and extremities, may be present. The best results will be obtained from the sensory examination if the tests are done with the patient's eyes closed. Finer tests for muscle coordination should also be done with the patient's eyes closed. The finger-to-nose test and the heel-to-knee test can be easily carried out, and both are very informative.

To summarize the foregoing discussion of signs and symptoms: It may be assumed that the patient is doing well if the pulse, respirations, temperature and blood pressure are not fluctuating, if stupor is lessening and if there is no progression in the neurologic signs. On the contrary, if the stupor is deepening, the pulse, respirations and blood pressure are fluctuating and there are signs of progressive central nervous system dysfunction, the patient's condition is deteriorating and unless something can be done to change the sequence of events, the outcome probably will be fatal.

After the status of the central nervous system has been thoroughly evaluated, other associated injuries must be considered. If there is fracture of the extremities, at least emergency splinting must be done even in cases in which the head injury is severe, although whether or not to begin definitive treatment of complicated fractures depends, of course, upon the condition of the patient. The examiner ought also to attempt to determine whether or not there are any visceral injuries.

There are a few special procedures that are necessary to ascertain the condition of the patient soon after the head injury has occurred. If for any reason there is doubt regarding the presence of brain contusion, a spinal puncture should be done. The spinal fluid pressure should be measured with a manometer and the character of the fluid noted. If brain contusion has occurred, the fluid is usually blood-tinged or frankly bloody and there may be an increase in intracranial pressure. If the spinal fluid is clear and the pressure high, great care should be exercised in the withdrawal of more than a few drops of spinal fluid. In the absence of depressed fractures or penetrating wounds of the skull, the taking of x-ray films is not ordinarily necessary as an emergency procedure. In most instances, it is desirable to defer routine x-ray examination of the skull until the general condition of the patient is reasonably stable. In most instances, if a depressed fracture or a linear fracture crossing the middle meningeal channels in the temporal bone is present, it is observable in a scout film taken with a portable x-ray unit.

The use of electroencephalograms, pneumoencephalograms and angiograms is not necessary in the acute stage of head injury. Such examinations, however, are valuable in evaluating some of the post-traumatic states and late complications that occasionally occur.

TREATMENT

Treatment of acute head injury is usually started by treatment of the initial shock. Infusion of glucose solution, blood plasma and whole blood, administration of oxygen and stimulants and the application of external heat must be carried out irrespective of the head injury. After the initial phase of shock has subsided, and the type and extent of damage to the nervous system has been determined, more definitive treatment can be instituted.

One of the most troublesome symptoms is restlessness. That which is caused by cortical irritation alone is not common except in alcoholic patients, and usually there is good response to paraldehyde given by mouth or rectally. Some physicians give the drug intramuscularly and a few intravenously without apparent deleterious effects. In most instances, restlessness is due to pain and discomfort. This can be combated by adequate splinting of fractures, by comfortable positions in bed, by catheterization if the bladder is over-distended, and by giving appropriate analgesics. Codeine is probably the most helpful drug for the control of pain. Demerol® in doses not to exceed 100 mg. hypodermically, every three or four hours, may be used. Morphine, Pantopon® and Dilaudid® are not usually desirable

because of the depressing effect of these drugs on the respiratory mechanism, although they are usually tolerated well by persons with minor head injuries.

The routine use of chemotherapy and antibiotics is not justifiable. If the patient obviously has infection of the sinuses or ears and there has been a basal skull fracture with bleeding into the infected area, the necessity for antibiotics is apparent. In most cases, however, such therapy is not used prophylactically but is reserved until there is some evidence of the beginning of infectious process.

Enough fluid to maintain normal fluid balance should be given—a minimum of 1,500 cc. Usually five or ten per cent solution of glucose and water suffices. Except for cases in which there is a long period of unconsciousness, the maintenance of normal protein intake is usually not a problem. If it is apparent that the patient is going to have a very long period of stupor, a stomach tube can be used to insure adequate supplies of proteins and carbohydrates and electrolytes.

If the patient is unconscious, care must be taken to assure a free airway. The optimum position for the unconscious patient is a modified Sim's position to allow free drainage of secretions from the nose and throat. If this is not adequate, pharyngeal suction is necessary, and in some instances it is necessary to insert an intratracheal tube to facilitate aspiration of the bronchial tree. If an intratracheal tube is not practical, an intratracheal catheter can usually be inserted without difficulty in a deeply stuporous patient.

Oxygen therapy is of considerable value in all cases of serious head injury. As an emergency measure, a nasal catheter is more desirable than an oxygen mask. An oxygen tent with adequate refrigeration is usually very well tolerated after the patient has stabilized. In all cases, it is very important to humidify the oxygen adequately.

It is necessary to be continuously on the alert for rapid increases in the patient's temperature. Routinely, specific measures should be instituted before the rectal temperature reaches 104°. Ice bags on the head, axillae and groins should be used freely. Continuous administration of cooled and humidified oxygen is essential. Tepid sponges, sponges with ice water or with chilled alcohol are helpful. If the temperature is very high or is rising rapidly, so drastic a measure as sponging with ether is justified. In such an emergency, some measures are usually necessary to reduce intracranial pressure. If the pressure is elevated due to generalized cerebral contusion and edema, 50 per cent glucose solution given intravenously in 100 cc. doses may be helpful. Curiously, blood plasma seems equally beneficial. Spinal puncture may be done for transient reduction of intracranial pressure. If a rise in temperature is accompanied by progressive focal neurologic signs, it is because localized bleeding has occurred, and surgical intervention then is necessary.

In recent years, early ambulation has been prescribed for patients with injury of the head. In general, the author permits patients to become ambulatory as soon as they can be up and about without exaggeration of existing symptoms or production of new symptoms.

Certain complications of head injury must be kept in mind during the convalescent period. These include epidural or middle meningeal hemorrhage, acute and chronic subdural hematoma, intracerebral hemorrhage or so-called late traumatic apoplexy, delayed subarachnoid hemorrhage, convulsive seizure due to localized cortical cicatrix, and the very annoying but self-limited post-traumatic syndromes.

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Dermatitis of the Hands in Industry

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SUMMARY

Three hundred and twenty-eight patients were referred for opinion as to whether a dermatologic condition was due to occupational causes. The answer was affirmative in two-thirds of the cases.

Of 2,260 patients seen in ordinary private dermatological practice, about 9 per cent had lesions on the hands. Of 128 patients with contact dermatitis considered to be of industrial origin, 121, or 94.5 per cent, had lesions on the hands.

Establishing industrial responsibility in cases of suspected occupational dermatitis of the hands is difficult, but in most cases a just conclusion can be reached by following certain guides.

IF a case of dermatitis is caused by a substance to which the patient is exposed in his work, the fact is usually manifest in the location and type of lesions present and in data from a carefully taken history. As is to be expected, the hands and forearms are the most frequently involved areas, since in many industries the hands are likely to come into contact with substances which are either primary irritants or sensitizing agents. Primary irritants are strong chemicals, such as concentrated acids or alkalies, which injure the skin on contact. There are many other substances, such as plastics, dyes and drugs, which produce lesions—by allergic reaction—only after sensitization has occurred.

Often a physician is called upon to decide whether dermatitis is occupational in origin. The answer is in the affirmative if there is reasonable evidence that it has been produced by irritants met with in the claimant's work or that some preexisting eruption has been aggravated by these contacts.

In many instances of dermatitis of the hands the cause is obscure and the condition may be resistant to treatment. These difficult cases cannot be accurately diagnosed or classified without thorough knowledge of those dermatoses which commonly occur on the hands. The complexity of this problem can be appreciated by studying the reports of Wise and Wolff,[13, 14] Callaway and Barefoot,[3] Ayres and Anderson,[1] Downing,[4] Lane et al.,[5] Peck et al.,[7] Blaisdell and Swartz,[2] Rowe,[8] Sulzberger and Baer,[10] and Livingood and Pillsbury.[6]

Presented before the Section on Industrial Medicine and Surgery at the 80th Annual Session of the California Medical Association, Los Angeles, May 13-16, 1951.

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It is often most difficult to state definitely that a condition is non-industrial in cause. Many physisicians with an industrial practice adopt theories which make the decision easier, even though adequate proof of the etiologic factors may not be present in the case in question. The concept of the role of dermatophytosis and the dermatophytid in producing hand eruptions, which was propounded by Williams[12] in 1926, is an example of such a theory. Williams stated that persons with superficial mycotic infections of the feet often become sensitized to the products of the fungus and that vesicular eruptions of the hands occur because of absorption of these substances from the foci on the feet. This theory is still held to be valid; but in the early enthusiasm for it, industrial physicians had a tendency to regard all vesicular or eczematous eruptions of the hands as dermatophytid reactions if the patient had dermatophytosis of the feet. Inasmuch as the large majority of adults have chronic dermatophytosis of the toes, it can be easily seen how this occurred. The authors agree with Wise and Wolff[14] that "among the rank and file of practitioners the tendency to make false interpretations of these simultaneous eruptions on the feet and hands has become far too prevalent. This explanation [the dermatophytid theory] is delightfully simple; all it lacks is confirmation." It is well to adopt a cautious attitude toward new explanations or theories, such as those ascribing vitamin deficiencies and allergic reaction to foods as the cause of eruptions on the hands, and to demand adequate proof before making binding decisions in given cases.

The present study is based on observation of 328 patients with dermatitis who were referred to the authors in the four years 1946-1949 for opinion as to whether or not the disease was of industrial origin. In 218 cases, about two-thirds of the total, the opinion given was that the dermatosis was caused by industrial exposure factors.

Of the 218 patients with dermatitis considered industrial in origin, 128 (59 per cent) had contact dermatitis due to sensitization or primary irritation from substances contacted during their work (Table 1). Of the 128 patients in this group, 121 (94.5 per cent) had involvement of the hands and forearms, and 83 (65 per cent) had no other involvement. These figures emphasize the need for a thorough knowledge of dermatoses of the hands in industrial dermatologic practice.

The patients with eruptions of industrial origin were employed in 58 different occupations. Table 2 lists the occupations in which there were three or more patients. Other patients were cosmeticians, leather workers, dentists, cannery workers, food handlers, etc.

TABLE 1.—*Diagnoses in 218 Cases of Dermatosis of Industrial Origin*

Diagnosis	No. Cases
Contact dermatitis	128
Hands and forearms	83
Hands and other areas	38
Hands not involved	7
Infectious eczematoid dermatitis or pyoderma secondary to industrial injuries	52
Chronic paronychia	11
Dermatitis medicamentosa secondary to treatment of industrial injuries	16
Dermatophytosis	3
Miscellaneous	8

TABLE 2.—*Type of Work Done by 120 Patients With Eruptions of Occupational Origin (most common, in order of frequency)*

Occupation	No. Patients
Cook	13
Painter	12
Mechanic	10
Brewery worker	10
Dishwasher	10
Domestic worker	9
Janitor	7
Teamster	6
Photographer	6
Printer	5
Carpenter	5
Candy maker	5
Florist	5
Cleaner	4
Baker	4
Bartender	3
Waitress	3
Lubricator	3

Table 3 indicates the wide variety of conditions which workers and their employers often suspect to be industrial in origin. It is of interest that a positive diagnosis of dermatophytosis of the feet with a dermatophytid reaction of the hands was made in only 11 patients (3.3 per cent) of the entire group referred for opinion. These patients, however, make up 10 per cent of the group with lesions considered non-industrial in cause.

COMPARISON OF PATIENTS IN THE USUAL PRIVATE PRACTICE AND THOSE IN INDUSTRIAL PRACTICE

As was previously noted, 94.5 per cent of 128 referred patients with contact dermatitis of industrial origin had involvement of the hands and forearms. Of 2,260 patients observed in private practice during the same period, only 9 per cent had dermatologic lesions on the hands.

Sixteen different kinds of dermatosis were diagnosed in a series of 201 patients in private practice who had lesions of the hands alone or of the hands and other parts of the body (Table 4). There are, of course, other conditions which may affect the hands and which were not included in this study. These include granuloma annulare, deep fungous infections, syphilis, leprosy, lupus erythematosus, lupus vulgaris, sarcoidosis, xanthomatosis, epithelioma, verruca, and others.

TABLE 3.—*Diagnosis in 110 Cases of Dermatosis Considered Non-Occupational*

Diagnosis	No. Cases
Generalized dermatitis of internal origin	18
Dermatophytosis with dermatophytid reactions of the hands	11
Contact dermatitis	18
Scabies	11
Herpes zoster	6
Seborrheic dermatitis	5
Miscellaneous (Pityriasis rosea, furunculosis, urticaria, eczema, pernio, acne rosacea, herpes simplex, keratoses, etc.)	41

The number of possible causative conditions indicates the complexity of the problem of differential diagnosis of eruptions of the hands. Although it is beyond the scope of this paper to attempt a detailed discussion of the differential diagnosis of eruptions of the hands, a few words should be said concerning the most common and most baffling of these lesions, namely, vesicular and eczematous eruptions of the hands. These eruptions are frequently obscure in origin and therefore are difficult both to diagnose and to treat, particularly in patients seen in ordinary private practice. Many physicians, and the majority of dermatologists, agree that a differential diagnosis cannot be made on clinical appearances alone. At times, as was suggested by the work of Waldbott and Shea,[11] the distribution or the pattern of the lesions will lead to discovery of the causative agent of a contact dermatitis. In other instances, the kind of lesions and the distribution will suggest a dermatophytid reaction. The influence of vasomotor instability or psychogenic factors will be apparent in some cases. It is also possible for a combination of causes to produce the eruption.[10] As the morphologic features of the lesions are rarely diagnostic, all the known etiologic elements must be analyzed in each case; even then, in many cases the origin will remain obscure.

Despite the numerous conditions which may affect the hands, the determination as to whether an eruption of the hands has been produced or aggravated by substances contacted in the patient's work need not be too difficult.

EVALUATION OF THE INDUSTRIAL NATURE OF ERUPTIONS OF THE HANDS

The evaluation of an eruption of the skin to determine whether it is of occupational origin requires (1) some knowledge or understanding of the conditions of the occupation, (2) a careful history, (3) a complete examination of the skin, and (4) the use of at least two specific procedures: (a) microscopic and cultural methods for detecting fungi and (b) the skin patch test.

TABLE 4.—*Causes of Eruptions of the Hand in 201 Cases Observed in Private Practice*

Diagnosis	No. Cases
Contact dermatitis	68
Eczematoid dermatitis (unclassified)	45
Dermatophytids	27
Infectious eczematoid dermatitis	13
Atopic dermatitis	8
Dermophytosis (primary)	8
Scabies	7
Nummular eczema	6
Toxic dermatitis, internal origin	5
Localized neurodermatitis	4
Chronic paronychia	4
Seborrheic dermatitis	2
Psoriasis	1
Dyshidrosis	1
Arsenical keratoses	1
Tuberculid	1

1. The physician must know (a) what skin irritants are involved in an occupation, (b) whether such irritants can produce the type of eruption in question, (c) how and where exposure takes place at work, and (d) whether the distribution of the eruption is compatible with the exposure.

2. Certain points in the history must be brought out: (a) Was the patient free of the eruption before starting the occupation? (Aggravation of a pre-existing eruption may be an exception.) (b) Was there a correct time-relationship between exposure and the development of the eruption? (c) Are there other workers in a similar occupation and exposure who have similar skin eruptions? (d) Are the areas of the eruption at the sites of maximum exposure? (e) Are there outside non-occupational exposures? (f) And most significant, did the eruption first occur after contact with the agent or agents in question, improve after cessation of exposure, and then flare again or recur after re-contact with the agents?

3. Examination of the entire skin surface is important and should be routine in every case. Information may be obtained which will assist in determining the occupational nature of the eruption. Exposed body surfaces are usually the common sites for lesions of industrial origin, but the covered parts of the body may be involved by indirect contamination, by contact with the hands, by penetration through the clothing, or by internal absorption. Friction of the clothing alone may be an important factor to consider. Complete information may give further knowledge of the distribution of the eruption.

Not only the distribution but the character of the eruption is important in determining the occupational aspect of the condition. Eczematous eruptions, either from primary irritants or skin allergens, are the common lesions, although paronychia, keratoses, folliculitis and acne-like disorders are occasionally industrial in origin.

4. Most eczematous eruptions are due to primary skin irritants; from 15 to 20 per cent arise from specific skin allergens or skin sensitizers.[9] The use of the skin patch test for determining specific sensitizing substances is essential for the diagnosis of the latter eruptions.

In doing the patch test, it is important to avoid using a substance in a concentration known to be a primary irritant. There are publications which list the substances,[9] giving the proper concentrations for use, the vehicles, and the time they should be left on the skin in order to distinguish hypersensitivity from primary irritation.

The patch material commonly used consists of a piece of adhesive plaster about one and one-quarter inches wide, with a somewhat smaller central section of cellophane. The substance to be tested is applied to a piece of gauze or smooth white cotton sheeting about three-quarters of an inch square. As adhesive material frequently produces dermatitis, it is important to have the testing substance separated by a sufficient margin from the adhesive plaster so that confusion in reading the reaction may be avoided. The gauze or cotton square is then moistened slightly, but not saturated, with the liquid substance to be tested. If powders or scrapings are used, they are applied to the gauze after it has been slightly dampened with water. Fabrics and solid material, such as rubber, metal, plastics, etc., may be dampened and applied in place of the gauze.

The patches must be applied to an area of normal skin. They are best placed on convex surfaces, usually on the arm, the back or possibly the thigh. Concave areas, such as those of the mid-back and shoulder, are not recommended. It is advisable to use additional strips of adhesive tape to keep the patch in firm contact with the skin. Scotch tape may be substituted when sensitivity to adhesive plaster is known to exist. The patches are left in place and kept dry for 24 to 48 hours, but not over 96 hours. It must be remembered that sweating and heat will hasten a reaction. The patient should be advised to remove the patches or return for observation if excessive itching or any burning occurs.

The typical positive reaction to a skin sensitizer is a fairly sharply demarcated, red, edematous and vesicular itching spot. The reaction may vary in degree from mild erythema to bullous formation. In contrast, a moderate reaction to a primary irritant tends to be erythema with less edema; the site is less raised and there may be little or no itching. The superficial layers of the skin may be slipped off by the finger, leaving a moist area. A severe reaction from primary irritation may occur as a sharply outlined blister or a necrotic ulcerated area with relatively little edema and vesiculation. Burning instead of severe itching may be present. Allergic reaction tends to become more pronounced during the day following removal of the patches, whereas reaction from primary irritation tends to remain the same or to improve. Thus, if reaction is questionable, the patient should be observed one or two days after removal of the patches. Erythema from adhesive plaster also may disappear during this period.

Care must be taken that patch tests are not made:

(1) on patients with acutely developing skin eruptions, (2) with unknown substances until they are standardized, (3) with the wrong vehicle, (4) on an exposed skin area where a prolonged reaction may result, (5) with primary irritants, and (6) with the wrong concentration.

In some circumstances there may be negative reaction even though the patient has sensitivity to the agent tested: (1) the area tested may be too remote from a localized site of skin sensitivity; (2) the patient may be in a so-called refractory phase of sensitivity; (3) the test may not be adequate to reproduce the conditions met with in the occupation. Neither a positive nor negative reaction is significant unless it coincides with the clinical data. The most significant criteria are that the eruption develops on exposure to the substance in question, subsides when exposure is eliminated, and flares again on reexposure to the substance.

TREATMENT OF CONTACT DERMATITIS PRODUCED BY IRRITANTS MET WITH IN INDUSTRY

1. *Preventive.* In almost all industries workers may come in contact with substances which act as primary irritants or sensitizers of the skin. Workers in certain occupations, such as painters, those engaged in the manufacture or the use of a large variety of chemicals, photographers, lithographers, cosmeticians, those who handle greases and oils, janitorial workers, printers, cannery workers, food handlers and many others, are more liable to have such lesions than are salespeople, clerical workers, elevator operators, transportation workers, and the like. In industries where contact irritations are likely to occur, every effort should be made to prevent unnecessary exposure to these substances. Certain workmen, such as electric battery workers, should wear rubber gloves. A cotton glove should be worn next to the skin to avoid sensitization to the rubber itself and to prevent maceration of the skin. Harsh and abrasive soaps for cleaning the skin should be avoided. Irritating solvents should not be used. A protective cream, such as lanolin or boric acid ointment, is helpful.

2. *Active Treatment.* In treating dermatitis, the most common mistakes made are over-treatment and the application of remedies which in themselves may be irritating or sensitizing. A strong mercurial, salicylic acid, or tar preparation may make the eruption much worse and increase the patient's disability greatly. Preparations containing sulfathiazole, penicillin, butesin picrate, etc., may produce allergic or sensitization reactions and again prolong disability.

In treating acute dermatitis of industrial origin the authors use wet dressings. A solution of aluminum acetate, diluted 1:15 to 1:20, is frequently used as a continuous cold wet dressing. Hand baths in a solution of lukewarm boric acid or potassium permanganate, diluted 1:5000, three times daily, for one-half hour, are used if there is evidence of secondary pyogenic infection. In the interim between hand baths, a mildly antiseptic lotion, such as 5 per cent tincture of Metaphen® in calamine lotion, is applied. Greases, such as ointments, pastes, and other oil-containing bases, are never used until the acute phase of the eruption has passed.

Antibiotics are given when secondary pyogenic infection, resulting in lymphangitis and adenitis, is present. Penicillin, streptomycin, and aureomycin are not used locally because of the sensitizing qualities of these substances. Bacitracin and tyrothricin may be used locally, although they accomplish no more than does a mild preparation of the time-honored ammoniated mercury.

Therapy with x-ray or cold quartz ultraviolet light is a useful adjunct in the treatment of these conditions, if used judiciously.

In addition to local therapy, at times it is necessary to treat the general condition of the patient, especially when dealing with elderly persons and persons with nutritional or systemic disturbances.

3. *Prognosis.* Contact dermatitis of occupational origin usually clears within a few weeks, providing the patient avoids contact with the causative substances and if proper treatment is given. A group of 34 patients with contact dermatitis was studied to determine the length of time required for the condition to clear. The time varied from one to 36 weeks: In 11 patients, ten weeks or more was required; in the remaining 23, six or less weeks was necessary. The patients who improved more slowly were those in whom the eruption involved other parts of the body in addition to the hands.

Recurrences are common if the patient returns to his previous occupation without taking adequate precautions to avoid further contact with the sensitizing substances. Workers who have had true sensitization reactions are more liable to have recurrence than are those with eruptions due to primary irritants.

The prognosis for dermatitis of industrial origin may be affected by the age and general health of the patient. The condition is often more resistant to treatment and improvement is slower in elderly people and those below par physically than in younger and more physically fit individuals.

The prognosis is greatly changed when localized dermatitis of the hand becomes widespread and extensive. Patients in whom this kind of absorption dermatitis develops are the most difficult to treat successfully. Repeated attacks of dermatitis often lead to the generalized form.

COMMENT

Dermatosis of industrial origin is probably the most common cause of disability in industry. According to Schwartz,[9] approximately 65 per cent of all industrial disabilities are dermatological. The importance of correct early diagnosis and proper treatment of these injuries is obvious. Much suffering, lost man-hours of work, and financial loss thus may be avoided.

First-aid treatment at the plant should be limited to the simple remedies—only soothing lotions, wet dressings or mild antiseptics should be applied. If

the condition persists longer than a week, dermatological consultation should be sought. It is often impossible to determine accurately the industrial nature of a lesion if it has been irritated or altered by previous treatment. From the standpoint of the insurance carrier, an accurate diagnosis from the start is an economy.

The industrial physician must be careful in judging the nature of an eruption. It is far too easy to make a decision which may be unfair to the worker or to the insurance carrier. It does not appear just to state unequivocally that a skin eruption of the hands is due to allergic reaction to food, to dermatophytosis, or to vitamin deficiencies unless there is adequate proof. It is equally unjust to declare that generalized psoriasis, scabies, lichen planus or dermatitis contracted at home as a result of painting the house or repairing the automobile is of industrial origin.

It is particularly true in industrial medicine that the physician must constantly avoid prejudice, so that the parties concerned are not unfairly affected by inaccurate decisions.

450 Sutter Street.

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Discussion by WM. F. B. HARDING, M.D., *Sacramento*

All true occupational dermatoses are curable if the cause is removed and sufficient time is allowed to assist the skin to return to normal; and, except for hypersensitivity, the disability is never permanent. It follows then that the industrial patient must, in general, be treated until he is well. In the instance of simple contact dermatitis from a primary irritant, this reasoning should and does hold true.

Unfortunately, however, as Doctors Epstein and Allen have so aptly pointed out, other complicating factors frequently are present. Such conditions as a fungus infection (active or dormant) on the feet, hyperhidrosis and neurocirculatory dyshidrosis of the hands, and finally, a so-called (for want of a better term) eczematous or allergic tendency may be present. In some instances of workers with allergic sensitization to occupational exposures, a change of occupation is almost mandatory if they are to remain free of dermatitis. However, some persons with hypersensitivity gradually become desensitized while continuing the same kind of work.

The authors have pointed out the necessity for proper evaluation of complicating factors in deciding whether or not dermatitis of the hands is due to the patient's occupational exposures or is aggravated by them.

It is my experience that dermatitis that is aggravated by occupational exposures is often the most difficult to clear or cure. Certain underlying or preexisting factors, such as those just mentioned, may render cure unlikely or even practically impossible. In such circumstances, the patient and insurance carrier should be so advised and treatment terminated when it is felt that maximum improvement has been attained.

Every case of dermatitis of the hands is definitely an individual problem and generalizations as to diagnosis and treatment are to be avoided. The authors' criteria for the evaluation of the industrial nature of hand eruptions should be most helpful to those practicing industrial medicine. The importance of avoiding overtreatment of occupational dermatitis cannot be too strongly emphasized.

An employee with generalized or severe localized occupational dermatitis is an expensive liability. For their own welfare as well as that of the patient, employers and insurance carriers should make every effort not only to assure competent early diagnosis and treatment of suspected occupational dermatosis, but to educate employees to avoid self-treatment. In so doing, much loss of time from the job, loss of wages and prolongation of compensation can be avoided.

CASE REPORTS

Non-Tuberculous Psoas Abscess
Infectious Mononucleosis

Non-Tuberculous Psoas Abscess

CLIFFORD L. GRAVES, M.D., *San Diego*, and
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PSOAS abscesses are of two kinds, tuberculous and non-tuberculous. Most textbooks give the impression that the tuberculous abscesses are far the more common but Bahn[1] in 1943 reported that of 35 cases of psoas abscess observed at the Charity Hospital in New Orleans, 60 per cent were tuberculous and 40 per cent were non-tuberculous.

Because the diagnosis of non-tuberculous psoas abscess is so easily missed and because the condition receives very little attention in the current literature, the following case is reported.

REPORT OF A CASE

A 53-year-old white housewife complained of pain, of ten days' duration, in the right lower quadrant of the abdomen and the right leg. The onset of these symptoms followed a severe head cold. Three years earlier a similar attack had occurred. At that time the patient was hospitalized for a few days but no definite diagnosis was established. In the intervening years the patient had remained reasonably well although there were occasional attacks of pain in the right lower quadrant of the abdomen and down the leg. Treatment was not sought during these attacks. There were no associated symptoms referable to the gastrointestinal or the genito-urinary tract. On examination an ill-defined mass was palpated in the right lower quadrant of the abdomen. It extended from the flank to the groin and seemed to be retroperitoneal. The liver and the spleen could not be felt and the pelvic organs were normal to palpation. Motion of the right hip was free. There was slight pitting edema of the right leg without clinical evidence of thrombophlebitis. The heart and lungs were normal. Blood pressure was 110 mm. of mercury systolic and 80 mm. diastolic.

Results of urinalysis were within normal limits. In examination of the blood, moderate anemia was noted and leukocytes numbered 15,950. Result of a Wassermann test was negative for syphilis. No abnormality was observed in an x-ray film of the chest. In a film of the abdomen there was obliteration of the right psoas shadow. The lumbar spine was normal roentgenographically, both on anteroposterior and on lateral view. In barium studies the stomach and the upper intestinal tract were normal in appearance but a filling defect of the cecum and the ascending colon was observed. The impression was that of an extrinsic mass. In excretory urograms some downward displacement and rotation of the right kidney was noted. There was slight clouding of the costophrenic angle on the right.

The patient was febrile, with temperature elevations to 102° F. After one week of observation, operation was carried out. The provisional diagnosis was retroperitoneal abscess of undetermined origin. The incision extended from the tip of the last rib to the groin. There was a giant abscess in the retroperitoneal region, overlying the psoas and extending from the second lumbar vertebra to the groin. The cavity was as large as a fist and contained about a pint of thick, creamy pus. No organisms were observed in a smear of the pus, and none grew on a culture. The ascending colon, the cecum, and the appendix were carefully palpated through the peritoneum. No lesions were noted. The right kidney was also normal to palpation. The abscess was drained through a stab wound in the groin and the main incision was closed. A biopsy specimen from the wall of the abscess was reported as non-specific inflammatory tissue.

Roentgenogram with barium enema. Note the poor filling of the ascending colon because of pressure from the psoas abscess.

Convalescence was uneventful. All drainage stopped within three weeks and the patient felt well.

DISCUSSION

Pyogenic psoas abscess may be hematogenous, lymphogenous, traumatic, or idiopathic. It may also originate by direct spread from adjacent organs.

Hematogenous abscesses are those following puerperal sepsis and pneumonia. Lymphogenous abscesses result from breakdown and suppuration of lymph nodes under the psoas fascia. Traumatic abscesses start in a hematoma. Direct extension occurs from neighboring structures, particularly the kidney and the appendix, but also the colon, the pelvic organs, and even the ischiorectal fat.

It is interesting to speculate upon the etiologic classification of the case here reported and upon how long the abscess had been present. As the urine was normal, as no abnormality was observed in a urogram, and as the kidney was normal to palpation, it is improbable that the abscess was of renal origin. The intestinal tract was normal and so was the lumbosacral spine. Therefore, the common foci were not present there. In all probability, the lesion was lymphogenous, beginning from lymphadenitis of the psoas region three years previously, the nodes then gradually breaking down and forming a sterile abscess which remained dormant during the intervening years. Eventually, perhaps under the stimulus of upper respiratory tract infection, the abscess spread rapidly along the established anatomical planes, causing the symptoms noted.

In the acute phase, most of the salient features of pyogenic psoas abscess were present:

1. There was pain and a mass in the right lower quadrant of the abdomen, together with evidence of sepsis.

2. Fixation of the hip in flexion—a sign that occurred in 58 per cent of the cases reported by Bahn—was not present. Edema of the leg, which was not present in any of Bahn's patients, was noted in the present case. This edema was undoubtedly due to pressure on the pelvic veins.

3. There was roentgenologic evidence of a tumor pressing on the ascending colon and there was partial obliteration of the psoas shadow. The curvature of the spine that has been described in reports of psoas abscess was not present.

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Infectious Mononucleosis

With Report of Four Cases

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INFECTIOUS mononucleosis is of interest because it may simulate many other disease syndromes. Interest in the disease has also been stimulated by recent reports of fatalities[5, 11, 13] from what had been described previously as an invariably benign illness. It therefore seems worthwhile to review some of the protean manifestations of this disease.

Correct diagnosis is essential in differentiating this usually benign condition from such malignant diseases as acute leukemia. It may also be important in explaining such vague symptoms as weakness and fatigue.[2]

The diagnosis of mononucleosis depends on a high degree of suspicion on the part of the examining physician. The manifestations are protean because the characteristic perivascular infiltration of abnormal lymphocytes may occur in various organs and systems in different cases.[3]

The disease may present itself as a generalized illness or it may involve a particular system. The most common manifestations are summarized in Table 1. Each may occur alone, although combinations of the various types of symptoms are more usual.[17]

Anginose mononucleosis may be confused with ordinary "sore throat," with hemolytic streptococcal sore throat, or with diphtheria. The following case from the records of the University of California Hospital is typical.

CASE REPORT

CASE 1: A 27-year-old woman had severe sore throat, fever, and membranous pharyngitis suspicious enough to justify administration of diphtheria antitoxin. A leukocyte differential count of 61 per cent lymphocytes, including 20 per cent atypical cells, and a heterophil antibody titer of 1:3584 established a diagnosis of mononucleosis.

Fever commonly accompanies some of the other manifestations, although it may occur as the chief symptom. Thus, mononucleosis is one of the causes of "fever of undetermined origin." In the following two cases taken from the records of University of California Hospital, diagnoses of typhoid fever and bacterial endocarditis, respectively, were seriously considered until the true diagnosis of mononucleosis was established.

CASE REPORTS

CASE 2: A 26-year-old male dental student was admitted to the hospital the first day of a febrile illness. Lymph nodes and spleen did not become enlarged.

Positive agglutination with "H" and "O" antigens at 1:320 dilution, in association with leukopenia (3,600 leukocytes per cu. mm.), led to strong suspicion of typhoid fever. The patient became afebrile in the second week of illness, the lymphocytes increased to 44 per cent of the number of leukocytes, with several atypical forms, and the heterophil titer rose from 1:28 initially to 1:112. The patient was discharged from the hospital with a diagnosis of mononucleosis.

* * *

CASE 3: A 43-year-old male, who had had rheumatic fever repeatedly in childhood and had been followed in the cardiac clinic for aortic and mitral valvulitis, reported to the clinic with complaint of chills and fever of one week's duration. Because of the presence of splenomegaly and a single splinter hemorrhage, a diagnosis of subacute bacterial endocarditis was entertained and immediate hospitalization was arranged. There was no pathogenic bacterial growth on five blood cultures. The heterophil antibody titer was 1:448.

TABLE 1.—*Symptoms of Various Kinds of Infectious Mononucleosis*

Type	Symptoms
Anginose	Sore throat
Febrile	Chills, fever, sweats, malaise
Glandular	Tender, painful nodes
Pulmonary	Cough, chest pain, x-ray findings as in atypical pneumonia
Abdominal	Pain, nausea, vomiting
Hepatic	Anorexia, nausea, vomiting, icterus
Central nervous system	Headache, stiff neck, paralysis
Eruptive	Rash resembling rubella, scarlet fever, etc.
Insidious	Fatigue, malaise
Hemorrhagic	Bleeding
Tumorous	Tumefaction

From the Division of Medicine, University of California School of Medicine, San Francisco.

Presented before the Section on General Medicine at the 80th Annual Session of the California Medical Association, Los Angeles, May 13 to 16, 1951.

Fever and splenomegaly subsided spontaneously, and the patient was discharged 12 days later with a diagnosis of mononucleosis.

Glandular enlargement is such a common occurrence in this condition that the disease was originally described as glandular fever. The cervical nodes are most commonly affected, but the adenopathy may be generalized and is at times quite painful.

Although cough is common, demonstrable pulmonary involvement is rare. When present, the pulmonary lesion may simulate primary atypical pneumonia clinically and radiologically. In this connection, Seifert[9] noted cold agglutinin titers of 1:32 or higher (which are usually considered diagnostic of atypical pneumonia) in a high percentage of patients with mononucleosis who had no symptoms of pneumonia.

Mononucleosis of the abdominal type may closely simulate acute appendicitis or other abdominal conditions necessitating surgical treatment.[7] Spontaneous rupture of the spleen, which has been weakened by lymphocytic infiltration, dissolution of trabeculae, and thinning of the capsule, has been reported in several cases. It usually occurs in the third week of illness and at times is apparently precipitated by too vigorous palpation.[13, 15]

Hepatic mononucleosis has been the subject of several recent publications. It resembles ordinary infectious hepatitis, both clinically and pathologically. Almost every patient with mononucleosis has some diminution of liver function,[11] but only a few have clinical signs of jaundice.[16] The jaundice usually lasts about three weeks, although Abrams[1] described one patient with intense jaundice which persisted over 11 weeks. The following case is typical of mononucleosis of the hepatic type.

CASE REPORT

CASE 4: A 26-year-old male medical student had fever for one week and was then afebrile for two weeks in the hospital. Hepatomegaly developed. In a bromsulfalein test there was 6 per cent retention at one hour and a thymol turbidity test reading was 21 units (normal 0-7 units). Lymphocytosis (66 per cent, with 10 per cent atypical forms) and a heterophil titer of 1:1792 proved the hepatitis was associated with infectious mononucleosis.

Central nervous system involvement, with clinical manifestations of benign lymphocytic meningitis, encephalitis, peripheral neuropathy, Guillain-Barre syndrome, or bulbar poliomyelitis, has been described with increasing frequency in recent years.[12, 13] Slade[10] reported on two soldiers with mononucleosis who were discharged from the Army because of persistent nervous system damage. Other investigators have reported cases in which death resulted from respiratory paralysis. Piel[8] described a case of infectious mononucleosis complicated by serous meningitis, encephalomyelitis and bilateral papilledema. Dolgopol[5] has recommended determination of heterophil titer in all acute neurological conditions of obscure cause. Tidy[14] noted that clinical involvement of the nervous system may precede, accompany or follow the hematologic changes characteristic of mononucleosis.

Hemorrhagic manifestations are rare in mononucleosis and should ordinarily suggest another diagnosis, such as acute leukemia, but Dameshek[4] and Wallerstein and Madison[16] reported cases of mononucleosis with thrombopenia and purpura. Thompson[13] described frank hematuria as a manifestation of infectious mononucleosis.

Tumefaction, other than enlargement of nodes, spleen, or liver, is a rarity in this disease, but Lucia[6] described a patient with cauliflower-like growths on the cervix which were thought to be neoplastic but were found to be caused by mononucleosis. Subsequently the growths disappeared spontaneously.

The myocardium may be involved in mononucleosis. Electrocardiographic changes indicating myocarditis are known to occur. Focal myocarditis has been observed at autopsy, and in at least one case death was attributed to myocardial involvement.

Infectious mononucleosis should be considered in a variety of clinical pictures. The presence of characteristic hematologic changes or heterophil titer may confirm the diagnosis.

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California MEDICINE

OWNED AND PUBLISHED BY THE CALIFORNIA MEDICAL ASSOCIATION
450 SUTTER, SAN FRANCISCO 8 PHONE DOUGLAS 2-0062

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EDITORIAL

Medical Care on the March

This month the California Medical Association embarks on a program of medical public relations which is unique and which has already drawn nationwide attention.

The program is a composite result of several studies, including the report of physician-patient relationships by Ernest Dichter, Ph.D., the recommendations of the Advisory Planning Committee, the report of the Association's Committee on Medical Economics and numerous suggestions from county society offices which operate actively in the business administration in physicians' offices.

In its initial stages, this campaign will call for the dissemination of suggestions aimed at creating for the public two basic guarantees. First is the guarantee of the availability of medical care under any and all circumstances. This will include medical care at any time of the day or night, on any day of the year, and without regard to the ability of the patient to pay. Briefly summarized, it means "Medical care for all, regardless. . . ."*

This guarantee may sound like a big order but on analysis it comes down to little more than the organization of medical resources in the interest of the patient. At present the physicians in organized medicine in any community are actually delivering service on this basis to all the people of the community even though not by formally established procedure. When they can organize their own resources on an orderly basis, they can make a guarantee to the public that any person can receive medical care, regardless of circumstances.

The second guarantee to the public will be one of protection against possible abuses by physicians who are members of the American Medical Association. This will include protection against acts of malpractice, against unnecessary or incompetent procedure, against overcharges for service and against unethical acts by member physicians. Such protection is already given the public by the vast majority of physicians; the organized effort will be to protect the public from such acts by the few in the profession who may abuse their professional privileges.

Here, in a nutshell, is the program the C.M.A. is entering into. Its objectives are to prove to the public that the practice of medicine, so far as it is within the purview of the Association, is, in deed as well as in word, a service performed for the benefit of the public — to prove that member physicians honor the terms of the opening statement of the Principles of Medical Ethics, that "reward or financial gain is a subordinate consideration."

If the public is guaranteed the availability of high quality medical care under all circumstances, and if the public is guaranteed protection against ill-advised acts on the part of a few physicians, the public will take to its heart the reputable practitioners who make the guarantee and will reject any politically-inspired idea of dictatorial governmental medicine.

To implement this program and to assist all county medical societies in putting it into effect, the C.M.A. has employed two field representatives and has named its present field secretary as director of public relations. This constitutes a team of experienced men who can assist county societies and their members in earning the respect and admiration of their patients and of the residents in their communities, by performing in the highest traditions of the profession.

As time goes on, other facets of the proposed program will be put into effect, as authorized by the governing bodies of the C.M.A. Meanwhile, the start which is now being made will carry to the people of the state the message that medicine means business and means its services to be performed for the good of the people. The effect of this program, both on the profession and the public, is bound to be salutary.

*Phrase coined by the Alameda-Contra Costa Medical Association.

Letters to the Editor . . .

Incidence and Importance of Thyroid Cancer

Discussing discrepancies in the frequency of thyroid cancer reported by surgeons and surgical pathologists with that reported by internists and autopsy pathologists, George Crile Jr., in the article on thyroid cancer in the *Journal of Clinical Endocrinology* of September 1950, makes the following statement (page 1155): "Until a basic statistical research is carried out in which a large population group is studied for a lifetime and in which no patient is subjected to thyroidectomy, and all of the thyroids are examined by serial section at autopsy, we shall have no accurate knowledge of the incidence and significance of cancer of the thyroid or its relationship to benign types of goiter."

It would be rather difficult in these days of ready thyroid surgery for even minor anatomical abnormalities of the gland to find a sufficient number of patients to satisfy the conditions of the first clause in the above quotation. Prior to the early 1920's, however, there appeared publications both clinical and pathological, which do meet these requirements and which stress the infrequency of cancer of the thyroid as a clinical problem. For example, if one reads successive editions of Osler's "Principles and Practice of Medicine," one notes in the earlier editions from the first through the ninth of 1923 this statement regularly repeated under Thyroid Tumors: "Cancer and sarcoma, which are rare, have a surgical interest." It is not until the tenth edition of 1925, published shortly after thyroid surgery became a safer and hence more frequent procedure, that the following statement appears under Thyroid Tumors: "Malignant tumors are more common than statistics usually indicate. Two hundred seven cases were found in 16,558 thyroidectomies at the Mayo Clinic. . . ."

Of what clinical significance are these new-found pathologically determined "malignant" lesions if up to three years before, persons with the same but unoperated and undiscovered lesions rarely suffered difficulty from them? These figures can lead only to the unconscionable conclusion that only the operated frequently demonstrate thyroid carcinoma, while the unoperated rarely suffer from their thyroid "malignancies"! The writer's experience, dating back to 1928, of over 2,000 autopsies mostly upon middle-aged and older persons, without finding a single instance of thyroid cancer being even a remote factor in causing death, leads him to question the reported great frequency of clinically important forms of this disease.

The second clause in the quotation, relative to serial section of the thyroid at autopsy, brings up the point of the need for differentiation between lesions of the thyroid interpreted histologically as malignant and their implied seriousness as a clinical problem. Especially in the case of the thyroid, are these two not necessarily synonymous. Johnson (*Arch. Surg.*, 59:1088, 1949) examined 165 completely removed thyroid glands from autopsy material by sectioning them at 2 to 3 mm. intervals and found two unsuspected lesions interpreted as malignant. One wonders what the frequency of malignant lesions would have been had sections been made at 1 mm. intervals or less. Complete serial section of the glands might have revealed even more areas interpreted as malignant; but what clinical importance do these "malignancies" possess if a control group with the same but undiscovered lesions live out their normal life's span with evidence of clinical maligancy resulting from such lesions no more often than rarely? In other words, *dying* with a lesion is not necessarily synonymous with dying *from* that lesion.

Thus, clinical and pathological experience up to 1925 as exemplified by Osler's textbook may be taken to represent the frequency of clinically significant thyroid carcinoma, whereas the statistics of more recent years include the incidence of lesions interpreted histologically as malignant but which are not necessarily clinically so, unless, of course, there has been a recent sudden actual increase in the frequency of thyroid malignancy, which possibility is not supported by current autopsy statistics.

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NOTICES AND REPORTS

Executive Committee Minutes

Tentative Draft: Minutes of the 228th Executive Committee Meeting, San Francisco, August 15, 1951.

The meeting was called to order by Chairman Lum in the offices of the Association at 5:30 p.m., Wednesday, August 15, 1951.

Roll Call:

Present were President MacLean, President-Elect Alesen, Council Chairman Shipman, Speaker Charnock and Auditing Committee Chairman Lum, Editor Wilbur and Secretary-Treasurer Daniels.

Present by invitation were Executive Secretary Hunton, Legal Counsel Hassard, A.M.A. President John W. Cline, A.M.A. Board of Trustees Chairman Dwight H. Murray, and Drs. Garnett Cheney of San Francisco, T. Eric Reynolds of Oakland and John Garthe of Vallejo, representing their respective county medical societies.

1. *A.M.A. Interim Session—December 4-7, 1951:*

Discussion was held on the advisability of a dinner being given for the A.M.A. House of Delegates when the interim A.M.A. session is held in Los Angeles next December 4 to 7. It was agreed that this should be a matter for local determination by the physicians of Los Angeles County.

2. *Death of William Randolph Hearst:*

On motion regularly made and seconded, it was voted to send a message of condolence to the family of William Randolph Hearst on the occasion of his death and to offer a floral piece at the funeral rites.

3. *C.P.S. Fee Schedule Committee:*

Discussion was held on the advisability of adding more members, representing medical specialties, to the C.P.S. Fee Schedule Committee. On motion duly made and seconded, it was voted to leave the composition of the committee at the present level of eight members, with the understanding that the committee could call in any specialist representatives it deems needed.

Adjournment:

There being no further business to come before the meeting, it was adjourned.

DONALD D. LUM, M.D., *Chairman*
ALBERT C. DANIELS, M.D., *Secretary*

C. M. A. Public Relations

To carry out its new program of public relations, the California Medical Association has named Mr. Ed Clancy as Director of Public Relations. Mr. Clancy has served as field secretary of the Association for the past three years, prior to which time he was associated with the Association's public relations counsel.

Aiding Mr. Clancy in this important work will be Mr. Glenn W. Gillette, who for the past three years has served as executive secretary of the Fresno County Medical Society, and Mr. J. L. (Jerry) Pettis, recently assistant to the president of United Air Lines. Mr. Gillette will make his headquarters at the Association's San Francisco office and Mr. Pettis at the Los Angeles office, 417 South Hill Street.

This team of three experienced representatives has already developed a large amount of material for the assistance of county medical societies and their members. All three are on call at all times for the consideration and solution of public relations problems throughout the state. Their talents are expected to contribute materially to the public esteem of physicians and their societies.

Special Announcement

CALIFORNIA MEDICAL ASSOCIATION ANNUAL MEETING

Los Angeles, April 27-30, 1952

The 1952 Annual Session of the California Medical Association will be held in Los Angeles, Sunday, April 27, to Wednesday, April 30, inclusive.

PAPERS: If you have a paper you would like to have considered for presentation, it should be submitted to the appropriate section secretary (see list on this page).

SCIENTIFIC EXHIBITS: Limited space will be available for scientific exhibits. If you would like to apply for space, please write immediately to the office of the California Medical Association, 450 Sutter Street, San Francisco 8, for application blanks. Please indicate *exact* space requirements. No exhibit shown in 1951, and no individual who had an exhibit at the 1951 session, will be eligible until 1953. *No requests for space will be considered after December 1, 1951.*

MOTION PICTURES: There will be facilities available for motion pictures. If you would like to exhibit, send your application to Dr. A. E. Smith, 1930 Wilshire Boulevard, Los Angeles.

All applications for scientific exhibit space and for time on the scientific program should be transmitted as soon as possible. The deadline is December 1, 1951.

ALBERT C. DANIELS, *Chairman,*
Committee on Scientific Work

SECRETARIES OF SCIENTIFIC SECTIONS

Allergy
Grace M. Talbott,
909 Hyde St., San Francisco 9

Anesthesiology
Nevin H. Rupp,
Veterans Adm. Center, Los Angeles 25

Dermatology and Syphilology
Kenneth L. Stout,
9629 Brighton Way, Beverly Hills

Eye, Ear, Nose and Throat
Robert C. McNaught, Stanford University
School of Medicine, San Francisco 15

General Medicine
J. Malcolm Stratton,
2560 Bancroft Way, Berkeley 4

General Practice
Merlin L. Newkirk,
3224 Santa Ana, South Gate

General Surgery
Paul C. Samson,
2938 McClure Street, Oakland 9

Industrial Medicine and Surgery
Orris R. Myers,
525 Seventh Street, Eureka

Obstetrics and Gynecology
Donald W. deCarle,
2000 Van Ness Avenue, San Francisco 2

Pathology and Bacteriology
Charles M. Blumenfeld,
2907 J Street, Sacramento

Pediatrics
Alvin H. Jacobs,
2201 Webster Street, San Francisco

Psychiatry and Neurology
Cyril B. Courville,
1801 New Jersey Street, Los Angeles 23

Public Health
John R. Philp,
0170 Civic Center, San Diego 1

Radiology
Robert K. Arbuckle
Samuel Merritt Hospital, Oakland

Urology
Roger W. Barnes,
1216 Wilshire Boulevard, Los Angeles

Questions and Answers about C. P. S.

Question: Is it necessary for the assistant surgeon or the anesthetist to list a diagnosis when submitting a bill to C.P.S.?

Answer: Yes. All bills paid by C.P.S. should have a diagnosis. In the case of assistant surgeons or anesthetists, they can expedite payments by submitting a diagnosis with their bills.

Question: Under its new contracts C.P.S. provides three months' medical care for each condition (except several listed conditions for which one year's care is provided). Is the three-month period renewable yearly?

Answer: No, this provision for three months' care is not renewable; once exhausted it is no longer available.

Question: In treating veterans under the Home-Town Care Program, is it necessary to report the results of special procedures on both the new request-for-treatment form (53-C) and the billing form (53)?

Answer: No. The reporting on the request-for-treatment form (53-C) should be of a general nature to assist the authorization officer of the Veterans Administration in evaluating the veteran's present condition. Reports of special procedures, x-rays and laboratory tests, etc., should accompany the billing form (53).

Question: In the case of a C.P.S. patient who has two-visit deductible outpatient medical coverage (and thus is responsible himself for charges for the first two visits), if I see him only twice and then refer him to another physician, is it necessary for *me* to send a bill to C.P.S.?

Answer: Yes, because it is necessary for C.P.S. to have record of the first two visits before payment can be made for the third or any succeeding visit.

Question: How much progress has been made in converting the old C.P.S. contracts to the new contracts?

Answer: In Northern California this conversion process is virtually completed. In Southern California, as of July 31, approximately 50 per cent of the joint (C.P.S. and Blue Cross) contracts had been converted. Only the new contracts were offered for straight C.P.S. enrollments in Southern California, so no conversion of this business was necessary.

Question: Is it permissible for my secretary or office nurse to sign the statements for my services to veteran patients under the Home-Town Care Program?

Answer: No. Statements must be signed by the physician rendering treatment. A facsimile signature or signature of any person other than the physician rendering the treatment is not acceptable to the Veterans Administration.

Question: Is membership in the C.P.S. Individual Family Plan available at all times, or only during certain enrollment periods in certain areas?

Answer: Membership in the C.P.S. Individual Family Plan is available at all times, and in all areas, to those who qualify.

Question: The question concerns a C.P.S. patient who has medical-care-while-hospitalized. If this patient has been seen twice by the doctor prior to entering the hospital, will C.P.S. payment for medical services begin on the doctor's first visit in the hospital?

Answer: No. The medical-care-while-hospitalized contract provides that the member pays for the first two doctor visits to the hospital, with C.P.S. payment beginning with the third visit. The patient holding medical-care-while-hospitalized coverage is responsible for all medical care outside the hospital, plus the first two doctor visits after hospitalization.

Question: Please explain the "professional group" which C.P.S. has for doctors and their employees.

Answer: This "professional group" makes beneficiary membership in C.P.S. available to all physician members, as well as to their regular office employees—nurses, technicians, secretaries, receptionists, etc. The family dependents of the physician and of his staff employees also may be enrolled. Dues for membership in the "professional group" are handled on a direct payment basis and are payable quarterly, semi-annually or annually. The basic coverage provided is the surgical contract and the 50-day hospital contract. In addition, physician members and their staff employees may, if they desire, have either the two-visit deductible medical contract or medical-care-while-hospitalized; dependents, if they desire, may have medical-care-while-hospitalized. All who qualify may add catastrophic coverage.

Question: Does the Individual Family Plan provide for any outpatient medical service?

Answer: No. Individual Family Plan members are not eligible for outpatient medical service. The base coverage under the Individual Family Plan is surgical and hospital, with the option of adding medical-care-while-hospitalized.

Question: What are the qualifications to apply for enrollment in the Individual Family Plan?

Answer: The qualifications are that the person be under 60 years of age and a resident of California. It is not necessary to be employed or self-employed. The person may apply singly or with all eligible family dependents. Membership is dependent on satisfactory health statement.

NEWS and NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

The scientific program of the **American College of Chest Physicians,** to be held Sunday, December 2, in the Ambassador Hotel, Los Angeles, follows:

Morning Session

H. Brodie Stephens, San Francisco, moderator

The Mechanical Heart Apparatus—Sanford E. Leeds and Morris M. Culiner, San Francisco.

Pre- and Postoperative Cardiac Catheterization Findings in Mitral Stenosis—Richard S. Cosby, David C. Levinson, Willard Zinn, Sim P. Dimitroff, Robert Oblath, Varner Johns, Telfer Reynolds and George C. Griffith, Los Angeles.

Selection of Patients for Mitral Commissurotomy—George C. Griffith, Pasadena.

Surgical Treatment of Cardiac Valvular Stenosis—William H. Muller, Jr., Los Angeles.

The Etiology and Treatment of the Physiological Changes in Chronic Pulmonary Diseases—Burgess L. Gordon, Philadelphia.

The Nature of Electrocardiographic Changes in Coronary Artery Thrombosis: An Experimental Study—Clinton Shaw, Alfred Goldman, Eliot Corday, Joshua Fields, S. Rexford Kennamer, Inga Lindgren, Allen Smith and Myron Prinzmetal, Los Angeles.

Luncheon Round Table Discussions

1. Chemotherapy in Diseases of the Chest—Emil Bogen, Olive View, and Edward Dunner, St. Louis; moderator, J. J. Singer, Beverly Hills.
2. Cancer of the Lung—Lyman A. Brewer III, and Lewis W. Guiss, Los Angeles; moderator, Seymour M. Farber, San Francisco.
3. Modern Management of Pulmonary Tuberculosis—Reginal H. Smart, Los Angeles, W. L. Rogers, San Francisco, and James S. Edlin, New York; moderator, Chesley Bush, Berkeley.

Afternoon Session

J. Winthrop Peabody, Washington, D.C., moderator

100 Cases of Spontaneous Pneumothorax—Robert Walters, John N. Briggs and Francis X. Byron, Los Angeles.

Primary Tuberculosis in Adults—Jay Arthur Myers, Minneapolis.

The Significance of the Bronchopulmonary Segment—Chevalier L. Jackson, Philadelphia.

Pulmonary Histoplasmosis—Alfred Goldman, St. Louis.

Chemotherapy for Tuberculosis, Using Minimal Dosage Schedules—J. P. M. Black, San Fernando, and Emil Bogen, Olive View.

Pre- and Postoperative Pulmonary Function Studies in the Tuberculous Patient—Frank Cline, Jr., Seattle.

Dinner

Jane Skillen, Olive View, president, California Chapter, American College of Chest Physicians, presiding

Guest Speaker: Leo Eloesser, United Nations, New York City—Activities of the United Nations International Children's Emergency Fund.

X-Ray Conference

Burgess L. Gordon, Philadelphia, and Marcy L. Sussman, Phoenix. Moderator: David Salkin, San Fernando.

* * *

The **Research Study Club** of Los Angeles has announced its 21st annual midwinter postgraduate clinical convention in ophthalmology and otolaryngology, January 14 to 25, 1952. The course on ear, nose and throat will be held January 14 to 19; the course on the eye, January 21 to 25. A special course in Surgery of the Eye will be conducted January 18 to 20 by Dr. Meyer Weiner, emeritus professor of clinical ophthalmology, Washington University School of Medicine, St. Louis.

* * *

Twenty-eight students, 26 men and two women, were admitted to the first class to enter the University of California at Los Angeles School of Medicine. They were selected from 284 qualified applicants.

SAN FRANCISCO

Dr. Anthony J. J. Rourke, physician-superintendent of Stanford University Hospitals, was inducted as president of the American Hospital Association at the annual meeting of the organization, held last month in St. Louis. He succeeded Dr. Charles F. Wilinsky, director of Beth Israel Hospital, Boston.

As president of the association, Doctor Rourke will officially represent the American Hospital Association at a number of state, regional and other national hospital association meetings and will participate on the programs of conventions and conferences of related health organizations.

* * *

The 79th annual meeting of the **American Public Health Association,** the 18th annual meeting of the western branch of the association, and meetings of 13 related organizations will be held in San Francisco, October 29 to November 2. Dr. William P. Shepard of San Francisco, president of the association, will end his term in office and will be succeeded by Dr. Gaylord W. Anderson of Minneapolis.

* * *

The **American College of Surgeons** will hold its annual meeting in San Francisco, November 5 to 9.

* * *

Two members of the faculty of the University of California School of Medicine recently were advanced to full professorship and four to clinical professorship. Dr. Alex-

ander Simon was appointed professor of psychiatry and Dr. B. V. A. Low-Beer professor of radiology. The four new clinical professors are: Dr. T. Floyd Bell, obstetrics and gynecology; Dr. Michael Hogan, ophthalmology; Dr. Mary B. Olney, pediatrics; and Dr. Robert Wartenberg, neurology.

GENERAL

Schering Corporation of Bloomfield, New Jersey, has advised the A.M.A. Council on Pharmacy and Chemistry that a shipment of its ophthalmic preparation of **cortisone acetate** marketed under the trade name Cortogen Acetate Ophthalmic Suspension is **contaminated** with Pseudomonas aeruginosa organisms. Although only one batch of the material may be contaminated, the firm informed the Council that telegrams have been sent to all its wholesale and retail outlets, as well as to all ophthalmologists, in order to effect a complete recall of all shipments of the drug. "Physicians who have any Cortogen Acetate Ophthalmic Suspension on hand at this time would be well advised not to administer it to their patients," the Council said, adding that "Schering Corporation is to be commended for its prompt action which is in the best interests of the medical profession as well as the general public."

* * *

Two California towns, Pleasanton and Rio Vista, have been granted State Health Department permits to **fluoridate their public water supplies,** and the permits have been approved by the State Board of Public Health following assurance from the California Attorney General's office that the health department action is legally sound. Any other public or private water supplier may now request similar permission, the Health Department said.

* * *

The **American Bureau for Medical Aid to China,** which conducts a fellowship program for the training of Chinese physicians and nurses in modern American medical practice and aids Chinese medical personnel dislocated by Communists, is currently engaged in a campaign to inform the American public concerning the nature of its work and to enlist active financial support, according to recent announcement by Lt. General Albert C. Wedemeyer, U. S. Army (retired), a director the organization. A. B. M. A. C. was previously supported by funds allocated by the now inactive National War Fund and United Service to China. Besides the fellowship program, General Wedemeyer said, the principal functions of the organization are to aid special medical missions (on such diseases as malaria, trachoma, and tuberculosis) and to act as ground-breaker for the U. S. Economic Cooperation Administration.

A. B. M. A. C. headquarters are at 1790 Broadway, New York 19, N.Y.

* * *

Support for the campaign for funds by **United Red Feather Campaigns of America** was given by Dr. John W. Cline, president of the American Medical Association, in the following statement:

"The United Defense Fund fills a great need during this period of mobilization and military activity in Korea. It is sustained by contributions made to the United Red Feather Campaigns. The latter perform essential functions in the normal civilian life of our communities. These worthy projects depend upon money raised during the fall campaigns. They deserve the wholehearted support of physicians everywhere.

"More and more of our colleagues are being called into the armed forces. Our contributions will provide important services for them and at the same time assist us at home by extending the activities of voluntary hospitals, clinics, nursing services and other health agencies for citizens in the lower income groups.

"The medical profession has always advocated extension of medical and health services to these people by voluntary means. Private support will eliminate the hazard of governmental participation and control.

"The U.D.F. agencies are badly needed to care for the military through the U.S.O., to assist civilians in densely populated defense areas, to establish community projects through the U.C.D.S. and to provide clothing for the Koreans through A.R.K. These are splendid activities of great importance at the present time.

"This year, it is possible for us to subscribe to both the Red Feather home activities and the U.D.F. National Service Programs at one time. Let us get behind the Red Feather Campaign this year and make it a great success. We can render great service to our own communities and our armed services by so doing and can avoid the danger of government taking over these activities."

* * *

Programs for **postgraduate symposia on heart disease** to be held on the designated dates this month in San Diego, Los Angeles and San Francisco follow:

San Diego—October 15

Auditorium, U. S. Naval Hospital

MONDAY AFTERNOON

Presiding: Dr. Anthony Yuskis, President, San Diego County Heart Association.

1:30-1:45 p.m.—The Program and Aims of the San Diego County Heart Association—Anthony Yuskis, M.D.

1:45-2:00 p.m.—American Heart Association and Its Relations to State and Local Affiliates—Mr. Robert Titus, American Heart Association.

2:00-2:45 p.m.—Essential Hypertension—Francis Chamberlain, M.D., San Francisco.

2:45-3:30 p.m.—Correctable Congenital Heart Lesions; Diagnosis and Treatment—Louis Martin, M.D., Los Angeles.

3:30-4:15 p.m.—Rheumatic Fever, Its Diagnosis and Differential Diagnosis—George Griffith, M.D., Pasadena.

4:15-5:30 p.m.—Clinical-Pathological Conference: Congenital Cardiac Disease—Captain E. V. Jobe, presiding.

MONDAY EVENING

Manor Hotel

6:30 p.m.—Dinner.

8:00 p.m.—Angina Pectoris and Myocardial Infarction—Howard Sprague, M.D., Brookline, Mass.

Los Angeles—October 17, 18

Wilshire-Ebell Theatre

WEDNESDAY MORNING, OCTOBER 17

9:25-9:30 a.m.—Opening Remarks—Edward C. Rosenow, Jr., M.D., president, Los Angeles Heart Association.

9:30-9:45 a.m.—Primary and Secondary Polycythemia with Lung Volume and Arterial Oxygen Studies—Eugene J. Ellis, M.D.

9:45-10:00 a.m.—Third Annual Prize Essay.

10:00-10:20 a.m.—Dynamics of the Pulmonary Circulation—R. S. Cosby, M.D.

Intermission.

10:30-11:00 a.m.—The Significance of the Prominent Pulmonary Artery Segment—Marcy L. Sussman, M.D.

11:00-12:00 noon—The Heart in Chronic Pulmonary Disease—Dickinson W. Richards, Jr., M.D.

WEDNESDAY AFTERNOON

1:30-1:45 p.m.—Heparin Treatment of Angina Pectoris with Observations on the Two-Step Exercise Electrocardiograph—Hyman Engelberg, M.D.

1:45-2:00 p.m.—Elimination of Errors in Prothrombin Time Determinations with the Use of a Simple Control Test Applicable to Office Use—Arnold G. Ware, Ph.D.

2:00-2:15 p.m.—A Clinical Study of a Coronary Vasodilating Agent (Khellin)—Harold Miller, M.D.

2:15-3:15 p.m—Pattern of the Youthful "Coronary" Patient—Howard B. Sprague, M.D.

Intermission.

3:30-4:00 p.m.—Dynamic Significance of Cardiac Arrhythmias—Louis M. Katz, M.D.

4:00-5:00 p.m.—Round table discussion of Problems in the Management of Coronary Artery Disease—Moderator: Arthur M. Hoffman, M.D. Participants: Dickinson W. Richards, Jr., M.D., George W. Griffith, M.D., Howard B. Sprague, M.D., Eugene Levine, M.D., and Louis M. Katz, M.D.

ANNUAL DINNER

The Lounge of the Los Angeles County Medical Association

Guest speaker: Howard B. Sprague, M.D.

THURSDAY MORNING

9:30-9:45 a.m.—Case Findings and Techniques in Heart Disease—Edward Phillips, M.D.

9:45-10:00 a.m.—Evaluation of Thirteen Years of Patent Ductus Arteriosus Surgery—Sidney S. Sobin, M.D.

10:00-10:15 a.m.—Cardiovascular Effects of an Adrenalin-Like Compound (Vasoxyl)—Morris H. Nathanson, M.D.

Intermission.

10:30-11:00 a.m.—The Nature of the Wolfe-Parkinson-White Syndrome—Myron Prinzmetal, M.D.

11:00-12:00 noon—Mitral Commissurotomy: Indications for Surgery and Measurements of the Circulation Before and After Operation—Dickinson W. Richards, Jr., M.D.

THURSDAY AFTERNOON

1:30-2:30 p.m.—Diagnostic Challenges in Heart Disease—Howard B. Sprague, M.D.

2:30-3:00 p.m.—The Experimental Approach to the Etiology of Atherosclerosis—Louis M. Katz, M.D.

3:00-3:30 p.m.—Present Concepts and Status of the Relationship of Lipoproteins to Atherosclerosis—John W. Gofman, M.D.

Intermission.

3:40-4:00 p.m.—Electrolyte Hazards in the Treatment of Congestive Heart Failure—Helen E. Martin, M.D.

4:00-5:00 p.m.—Round table discussion of Dietary Aspects of the Management of Cardiovascular Diseases—Moderator: Lewis T. Bullock, M.D. Participants: Dickinson W. Richards, Jr., M.D., John W. Gofman, M.D., Howard B. Sprague, M.D., Helen E. Martin, M.D., and Louis M. Katz, M.D.

POSTGRADUATE EDUCATION NOTICES

UNIVERSITY OF CALIFORNIA SCHOOL OF MEDICINE—Medical Extension, Toland Hall, U. C. Hospital, San Francisco

Evening Symposia in Medicine:

Sept. 17-Dec. 17 (every Monday evening).

This is a series of evening exercises for practitioners in the form of symposia on t particular interest to them. Fee: $60.00.

Contact: Stacy R. Mettier, M.D., Medical Extension, U. C. Medical Center, San Francisco 22.

UNIVERSITY OF CALIFORNIA SCHOOL OF MEDICINE, Medical Extension, Los Angeles

OBSTETRICS AND GYNECOLOGY. October 17, 18 and 19—Intensive three-day course, 9:30 a.m. to 5:00 p.m. daily, School of Medicine, Los Angeles campus.

RECENT ADVANCES IN GENERAL SURGERY. Nov. 13-Feb. 11, 1952, 12 weekly evening lectures.

Guest Lecturers: Dr. Frank Glenn, Cornell University School of Medicine; Dr. Robert Elman, Washington University, St. Louis; Dr. Warren Cole, University of Illinois.

Contact: University of California Extension, Office of Medical Extension, Los Angeles 24.

MEDICAL STENOGRAPHY AND MEDICAL OFFICE PROCEDURES. Sept. 21 and 12 consecutive Friday meetings from 6:30 to 9:00 p.m. Extension Center, 813 S. Hill Street, Room 304.

San Francisco—October 24 to 27

Colonial Ballroom, St. Francis Hotel

WEDNESDAY MORNING, OCTOBER 24

9:00-12:15 p.m.—Course in Unipolar Electrocardiography—Presiding: Richard D. Friedlander, M.D.

9:00-9:30 a.m.—Fundamentals of Unipolar Electrocardiography—John B. Lagen, M.D.

9:30-10:00 a.m.—Normal Range and Variations—Arthur Selzer, M.D.

10:00-10:30 a.m.—Arrhythmias—J. K. Lewis, M.D.

Intermission.

10:45-11:15 a.m.—Ventricular Hypertrophy—Harold H. Rosenblum, M.D.

11:15-11:45 a.m.—Myocardial Infarction—Mervyn J. Goldman, M.D.

11:45-12:15 p.m.—Bundle Branch Block—Hilliard Katz, M.D.

WEDNESDAY AFTERNOON

1:30-5:00 p.m.—Heart Disease in Childhood—Presiding: Alice Potter, M.D., president, Northern California Pediatric Society.

1:30-1:55 p.m.—Brock Procedure: Indications and Results in Pediatrics—Sanford Leeds, M.D.

1:55-2:20 p.m.—Use of Unipolar Electrocardiography in the Diagnosis of Congenital Heart Disease—Maurice Sokolow, M.D.

2:20-3:30 p.m.—Cardiac Auscultation—A Panel Discussion.

Moderator: Ann Purdy, M.D.

Interpretation of Systolic Murmurs—Saul J. Robinson, M.D.

Interpretation of Diastolic Murmurs—C. R. Leininger, M.D.

Interpretation of Continuous Murmurs—Herbert N. Hultgren, M.D.

Phonocardiography—Howard B. Sprague, M.D.

Intermission.

3:45-4:10 p.m.—Psychic Impact of Heart Disease in Children—Hale F. Shirley, M.D.

4:10-4:35 p.m.—Current Status of ACTH-Cortisone Treatment of Rheumatic Fever—Vincent C. Kelley, M.D.

4:35-5:00 p.m.—Methods of Defining Rheumatic Activity—John A. Anderson, M.D.

Wednesday Evening

8:00 p.m.—Differentiation Between Cardiac, Pulmonary, and Functional Dyspnea—Dickinson W. Richards, Jr., M.D.

(This session is held in collaboration with the Medical Extension—University Extension—University of California Medical School, as one feature of a postgraduate series of 12 evening lectures in general medicine.)

Thursday Morning

Presiding: William L. Bender, M.D.

9:00-9:30 a.m.—Nonspecific Benign Pericarditis—Eli R. Movitt, M.D.

9:20-9:40 a.m.—Procaine Amide in the Prevention and Management of Arrhythmias—Arthur Twiss, M.D.

9:40-10:25 a.m.—The Dynamic Significance of Cardiac Arrhythmias—Louis N. Katz, M.D.

Intermission.

10:35-11:00 a.m.—Presidential address: Malignant Hypertension—Maurice Sokolow, M.D.

11:00-12:00 noon—Resistant Congestive Failure—Howard B. Sprague, M.D.

Thursday Afternoon

Presiding: Charles A. Noble, Jr., M.D.

1:30-1:55 p.m.—Varying Clinical Patterns of Mitral Stenosis—John J. Sampson, M.D.

1:55-2:50 p.m.—Mitral Commissurotomy: Indications for Surgery and Measurements of the Circulation Before and After Operation—Dickinson W. Richards, Jr., M.D.

2:50-3:15 p.m.—Surgical Aspects of Mitral Stenosis—Emile F. Holman, M.D.

Intermission.

3:30-5:00 p.m.—Medical and Surgical Aspects of Correctible Cardiovascular Lesions—A panel discussion—Moderator: Arthur Selzer, M.D. Participants: Robert H. Alway, M.D., Frank Gerbode, M.D., Herbert N. Hultgren, M.D., Henry D. Kaplan, M.D., Mary B. Olney, M.D., and H. Brodie Stephens, M.D.

Friday Morning

Chairman and Moderator: Lowell A. Rantz, M.D.

9:00-10:45 a.m.—Presentation of Selected Cases of Cardiovascular Problems, with Discussion of Diagnosis and Treatment.

Subacute Bacterial Endocarditis—Arthur L. Bloomfield, M.D.

Cardiovascular Side Effects of ACTH Therapy—John Luetscher, M.D.

The Abnormal Ballistocardiogram in Coronary Disease—Francis L. Chamberlain, M.D.

Cardiovascular Lues—Clayton D. Mote, M.D.

Intermission.

11:00-12:00 noon—The Heart in Chronic Pulmonary Disease—Dickinson W. Richards, Jr., M.D.

Friday Afternoon

Presiding: David A. Rytand, M.D.

1:30-2:30 p.m.—Pattern of the Youthful Coronary Patient—Howard B. Sprague, M.D.

2:30-3:00 p.m.—Experimental Approach to the Etiology of Atherosclerosis—Louis N. Katz, M.D.

Intermission.

3:10-4:35 p.m.—Arteriosclerosis and Its Sequelae—A panel discussion—Moderator: Louis N. Katz, M.D. Participants: John E. Adams, M.D., Ellen Brown, M.D., I. Lyon Chaikoff, M.D., Alvin Cox, M.D., John Gofman, M.D., Howard B. Sprague, M.D., and Edwin J. Wylie, M.D.

4:35-5:00 p.m.—Acute Arterial Occlusion—Norman E. Freeman, M.D.

Friday Evening

7:00 p.m.—Annual Dinner Meeting—Presiding: Maurice Sokolow, M.D., President.
Diagnostic Challenges of Heart Disease—Howard B. Sprague, M.D.

Saturday Morning

San Francisco Hospital

9:00 a.m.—Presentation of Patients with Various Types of Heart Disease—Presiding: J. Marion Read, M.D. Participants: Henry Brainerd, M.D., LeRoy H. Briggs, M.D., Roy Cohn, M.D., Maurice Eliaser, Jr., M.D., Peter H. Forsham, M.D., Rutherford S. Gilfillan, M.D., Marlow B. Harrison, M.D., Louis N. Katz, M.D., J. K. Lewis, M.D., Lester S. Lipsitch, M.D., Charles A. Noble, Jr., M.D., Dickinson W. Richards, Jr., M.D., Ernest Rogers, M.D., Arthur Selzer, M.D., Ben Shenson, M.D., Albert M. Snell, M.D., Howard B. Sprague, M.D., Norman J. Sweet, M.D., Clarence M. Tinsley, M.D., and Malcolm S. Watts, M.D.

INFORMATION

Change in Diagnostic Laboratory Service

Pathologists and other physicians in California who formerly sent specimens for special diagnostic services directly to the U. S. Public Service Communicable Disease Center Laboratories at Atlanta, Ga., are now required to direct all such specimens to the Division of Laboratories of the State Department of Public Health of California. This is in line with a change in policy effected by USPHS.

A letter from M. H. Merrill, M.D., Chief, Division of Laboratories, State Department of Public Health, advises that in view of the change in procedure, "physicians requiring special diagnostic work which is not available to them through their regular clinical or local public health laboratories should refer this work to the Division of Laboratories, 3093 Life Sciences Building, University of California, Berkeley. If our division is not able to provide such service, we shall take the responsibility of forwarding the specimens on to the Public Health Service."

Medical Care Costs Rise Far Less Than Other Family Budget Items

(Reprinted from *Capitol Clinic*, a newsletter issued by the Washington office of the American Medical Association.)

The American middle-income family is paying more for almost everything—but medical care costs are going up slower than any other major item in the family budget. This is reported by U. S. Bureau of Labor Statistics, based on its mid-1951 survey of living costs. (To obtain trends, BLS spot-checks prices of specific categories of goods and services; a number of union wage scales are tied to this survey.) The BLS report estimates medical care and drug costs in June at 54.7 per cent above the average for 1935-39. In contrast, clothing costs were up 104 per cent, house furnishings 112.5 per cent, household operations 61.7 per cent, recreation 68.3 per cent, personal care (such as haircuts, toilet goods) 93.69 per cent, and transportation 71.6 per cent.

This trend has been under way for some time. BLS, a Labor Department agency, estimated medical care and drug prices average 47.9 per cent above 1935-39 for all of 1950. Prices of most other goods and services last year ranged higher — in about the same proportion as prices of June of this year.

BLS gave this breakdown for June, compared with the pre-World War II average: All physicians' fees up 44.7; general practitioners' fees, 44.8; surgeons' and specialists' fees, 43.4; obstetrical fees, 65.2; dentists' fees, 59.4; hospital rates, 161.4; optometrists' fees, 34.9; prescriptions and drugs, 28.3. The survey showed that group hospitalization insurance had risen 2.9 per cent since December 1950, when the agency first began counting this item in its cost of living formula.

Medical care and drug costs were 54.7 per cent more than prewar, and medical care minus drug costs 60.5 per cent, in June. In contrast, food prices during the same period soared 126.8 per cent, or more than double medical care cost.

The BLS report complements the results of a recent national survey of physicians' incomes conducted by the Commerce Department and American Medical Association. It showed that increases in physicians' incomes since 1929 have been slightly below the increase for the general population.

Seventy-Five Per Cent of Korea Wounded Return to Duty

(Reprinted from *Capitol Clinic*)

Surgeon-General George Armstrong, back from a Korean inspection trip, reports Army Medical Department is functioning at a high rate of efficiency and contributing to troop morale. Among his findings:

1. Out of every 100 wounded men, an average of 75 eventually return to duty, 26 without leaving Korea, 35 more without leaving Japan and 14 after hospitalization in this country.

2. Death rate of wounded has been reduced to 2.5 per cent, in contrast to 4.5 per cent in World War II.

3. First aid is given in almost every case within 30 minutes; the exceptions, Gen. Armstrong learned from wounded, are generally confined to situations where the aid man attached to the unit also has been killed or wounded.

4. The new drug primaquine gives promise of becoming the first real cure for malaria; if it stands up under extensive testing, it should end the current problem of suppressed malaria breaking out after Korean veterans reach this country. The outbreaks, Gen. Armstrong believes, are not as serious as might be because of prompt and effective detection and treatment in this country.

BOOK REVIEWS

CORNELL CONFERENCES ON THERAPY — Volume Four. Edited by Harry Gold, M.D., Managing Editor, David P. Barr, M.D., McKeen Cattell, M.D., Frank Glenn, M.D., Walter Modell, M.D., and George Reader, M.D. The Macmillan Company, New York, 1951. 342 pages. $3.50.

Previous volumes of the Cornell Conferences on Therapy are undoubtedly familiar to many readers of this journal. This latest volume closely resembles the others in format and method of presentation. The emphasis is on practical aspects of therapy, although at times the discussion is quite theoretical. The editors are to be congratulated on presenting the material in such readable form, since transcriptions of unrehearsed conferences are very difficult to translate into formal presentations for publication. As one means of meeting this problem, the editors have concluded each discussion with a short summary of the various opinions presented. In an effort to be objective, these summaries occasionally do not reflect the degree of divergence of opinion that is apparent in the preceding comments. This is unfortunate on occasions where the speaker has been able to justify his point of view in a logical and thorough manner.

The sections dealing with household poisonings, treatment of diabetic emergencies, management of disorders of cardiac rhythm, medical management of hypertension, and treatment of morphine addiction contain much material of use to the general practitioner. Due to the rapid advances in scientific knowledge and the development of new therapeutic agents, any material published in book form is apt to be outdated, in part, when published. That the problem has not been surmounted in this volume is evidenced in the section on antimicrobials in genito-urinary infections.

The reviewer can recommend this volume for those physicians who desire a practical discussion of common therapeutic problems presented by the staff of one of our outstanding medical schools.

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GENETICS IN OPHTHALMOLOGY. By Arnold Sorsby, Research Professor in Ophthalmology, Royal College of Surgeons and Royal Eye Hospital, London. The C. V. Mosby Company, St. Louis. 1951. 251 pages. $9.50.

The author points out that, contrary to widespread belief, medical genetics is not concerned with collecting curious pedigrees of the unconsidered trifles of pathology but at the very least is an attempt to elucidate some of the constitutional bases of disease.

In England 50 per cent of blindness is due to cataract, glaucoma and senile macular degeneration. The majority of those afflicted with these conditions are over 60 years of age. Twenty per cent of blindness is due to myopia, congenital, hereditary and developmental defects. The majority of these persons are young or middle-aged; therefore these lesions rank first in terms of years as a cause of blindness.

The book is divided into three sections: (1) a theoretical discussion of the modes of inheritance in genetic diseases, (2) isolated ocular anomalies, and (3) generalized disorders with ocular aspects.

The theoretical discussion of the modes of inheritance and genetic diseases is briefly and very clearly written. This section will probably be of greatest value to the reader who is interested in establishing a pedigree for some ocular diseases. The sections on isolated ocular anomalies and generalized disorders with ocular lesions is well illustrated but the material is covered so briefly that it offers little more than can be found in many textbooks of ophthalmology.

This book deals with a narrow field in the specialty of ophthalmology. Its greatest assets are its illustrations and its defect is its brevity. The book will probably be used as a reference for those interested in ophthalmic and medical genetics.

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PHARMACOLOGIC PRINCIPLES OF MEDICAL PRACTICE—Second Edition—A Textbook on Pharmacology and Therapeutics for Medical Students, Physicians, and the Members of the Professions Allied to Medicine. By John C. Krantz, Jr., Professor of Pharmacology, School of Medicine, University of Maryland; and C. Jelleff Carr, Associate Professor of Pharmacology, School of Medicine, University of Maryland. The Williams and Wilkins Company, Baltimore, 1951. 1,116 pages. $10.00.

This second edition of a successful text has appeared only two years after the first edition, the popularity of which is indicated by the fact that it was reprinted four times during this period.

Aureomycin, chloramphenicol, and Terramycin have been added to the antibiotics chapter. Two new chapters have been added to the section on anti-infective drugs, i.e., one on "The Chemotherapy of Tuberculosis" with discussions of streptomycin, para-aminosalicylic acid, the sulfones (Promin, Diasone, and Promizole), and the thiosemicarbazones (Tibione), and the other a short chapter entitled "The Chemotherapy of Rickettsial Diseases." A brief chapter, "Anti-motion Sickness Drugs," has been included, and is devoted mainly to Dramamine. There is also a new chapter on the drugs used in the treatment of arthritis, devoted chiefly to cortisone and ACTH. The second edition includes the changes incorporated in the fourteenth revision of the "U. S. Pharmacopeia," the ninth edition of the "National Formulary," and "New and Nonofficial Remedies, 1950."

All important new drugs have been included together with references to their pharmacology and clinical use. A feature which appealed especially to the reviewer is the preliminary brief physiological discussion which often precedes the pharmacological section and which greatly facilitates a rapid understanding of the action of the drugs discussed. A serious attempt has been made to indicate mechanism of action for each class of drug, even though our knowledge of the events occurring at the cellular and sub-cellular level of organization is unfortunately very meager. References are given to recent research on mechanism of action for those readers who wish to supplement the necessarily brief discussions in the text. A table is given at the end of each chapter which lists the official preparations and dosages, but no indication is given in these tables as to whether the preparations are U.S.P. or N.F.

The only error noted by the reviewer was a reference to ergotoxine as an alkaloid of ergot (p. 899), without any mention of the discovery of Stoll that "ergotoxine" is actually a mixture of the three alkaloids of ergocornine, ergocristine, and ergocryptine. The reviewer believes that the section entitled "Social Aspects of Alcohol" contains a few statements that might be omitted from such a textbook, e.g., "But even social drinking has many adverse effects upon society. Among these are lowering of moral standards . . ." The general validity of such a statement is certainly questionable, and tends to detract from the otherwise scholarly tone of the book.

This work is generally very well written and authoritative, and contains much information not available in other texts. It is highly recommended to the medical profession and students.

THE ETHICAL BASIS OF MEDICAL PRACTICE. By Willard L. Sperry, Dean of the Harvard Divinity School. Paul B. Hoeber, Inc., 49 East 33rd Street, New York, N. Y., 1950. $2.50.

When a doctor of divinity, eminent and respected in his chosen field, with a background of many years of helpful and constructive experience in ministering to the mental and spiritual needs of our patients, sees fit to analyze the philosophical basis for our art and science he deserves a thoughtful and attentive hearing.

"The Ethical Basis of Medical Practice" presents in a book of 178 pages divided into 14 chapters the careful and studied conclusions of the dean of the Harvard Divinity School, and comprises in essence the subject matter of two addresses given by the author, one to the students of Harvard Medical School and the other the Roger Morris Lecture for the academic year 1948-49 at the Medical School of the University of Michigan.

The first chapter, "Our Overlapping Professions," indicates Dean Sperry's belief that medicine and the ministry have much in common, and that rather than be antagonistic to or suspicious of each other the representatives of each profession should strive to work harmoniously together in the recognition that the sick individual is in sum a human being with need for spiritual guidance as well as for physical restoration.

In the second chapter, "The Specialist and the General Practitioner," some broad general advice is given to the medical student or intern in the determination of whether to follow general practice or to enter one of the specialties. The author indicates that the minister must have a broad general knowledge of philosophy as well as a keen understanding of human nature in all of its manifestations. The implication is that if he were to specialize in one particular field he would lose his value to serve best the needs of his parishioners. The author's indication of the type of medical student best suited for general practice, and of the one most likely to serve best as a specialist is objective and helpful.

As a basis for evaluating medical ethics, Chapter III, "The Nature of Conscience," deals with fundamentals in the definition of morals, ethics, and conscience.

In Chapter V, "Professions in General," the author begins by emphasizing the theoretical difference between professions and trades and insists on the fact that trades are conducted for profit and professions are organized for service. The question of medical fees, a limited reference to the English system of compulsory health insurance, and some excellent examples of the value of professional ethics to the public, make this chapter particularly valuable. In subsequent chapters, codes of medical ethics are analyzed, quotations from the American Medical Association presented, and historical background indicated. The American tradition of the immediacy and intimacy of the relationship between doctor and patient is expressed as one of the basic fundamentals. By comparison with the ethical codes of ministers and lawyers, the author accords first place to the physician's code and the manner in which he lives it and defends it.

Having laid an excellent philosophic background for the code of medical ethics, the author now addresses himself to specific applications of that code and the difficulties these applications entail.

In Chapter VII, "Our Tragic Moral Choices," are presented some excellent illustrations, one of which is the conflict in which the physician finds himself when an apparently incurable patient requires repeated transfusions of a rare type of blood and the hospital laboratory indicates this rare type of blood should not be wasted on the hopeless patient but should be reserved for use on others whose lives might be saved. After considerable discussion, the author concludes that the true physician must continue to give the transfusions regardless of the apparent hopelessness of the patient under treatment. In a subsequent chapter in elaboration of this conclusion he states that the diagnosis of incurability in this instance was in error, that ultimately the patient so treated did recover.

Chapters headed "Democratic vs. Totalitarian Medicine," "Telling the Truth to the Patient" and "The Prolongation of Life," elaborate the author's fundamental belief in the value and dignity of each individual life, and the basic duty of the physician to preserve and prolong that life and make it as comfortable and happy as possible under any and all circumstances. This basic philosophy prepares the reader for the next two chapters—"Euthanasia—Pro," and "Euthanasia—Con." In "Euthanasia—Pro," there is a definition of the doctrine followed by a brief historical background which includes reference to the Greek attitude and that of primitive societies. A short modern history of the euthanasian movement is given with particular reference to the literature as supplied by the Euthanasian Society of America. In Chapter XII, "Euthanasia—Con," the author honestly and forcefully states his position in opposition to these proposals. He indicates the complications and dangers that might beset society were such a law on the statute books. He cites the corruption of medical ethics in Nazi Germany and refers to Dr. Ivy's article portraying medical crimes as practiced under the Nazi regime. He indicates the basic error of that regime was that the economic welfare of the state was considered of greater importance than the care of the individual patient, and upon that philosophical error the morale of the medical profession disintegrated. He sees in this fact the basic fallacy in the euthanasia philosophy which is that there is such a thing as a life not worth living. As a minister, he contends that all life has value. As a logical consequence of the basic principles of the euthanasia movement he visualizes a social system in which doctors of the army and navy, for example, would go through our veterans' hospitals and cull out the physical and mental misfits in the interest of economic efficiency.

The entire work is well written, studiously presented, and carefully documented as to sources. It leaves the physician-reader with an increased respect for the life of every individual patient under his care and the desire so to practice his art that each patient may indeed receive the care and consideration to which he is entitled as an individual human being and not as a cog in a collectivist machine.

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DIFFERENTIAL DIAGNOSIS OF INTERNAL DISEASES—Clinical Analysis and Synthesis of Symptoms and Signs. By Julius Bauer, M.D., F.A.C.P., Clinical Professor of Medicine, College of Medical Evangelists, Los Angeles. 866 pages. Grune and Stratton, New York, 1950. $12.00.

This large book on differential diagnosis demonstrates an exceedingly large fund of information and personal experiences on the part of the author. This is in keeping with what might be expected from his hospital and clinical background.

The unique feature of the book is the wealth of individual case reports with which the author documents the points that he wishes to emphasize in differential diagnosis. This is most useful and emphasizes the author's opinions in a way not possible with words alone. In the case reports and in the discussions, the author demonstrates a well-marked awareness of the importance of the emotions in disease and of psychosomatic correlations.

The author frequently refers to laboratory tests rather than to fine distinctions of symptoms or clinical course in

the differentiation of various disorders; this is the major criticism that the reviewer offers.

The book in general can be recommended as an interesting and personal discussion of differential diagnosis documented by case histories and reflecting largely continental opinion, although the American point of view is also presented.

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HANDBOOK OF PEDIATRIC MEDICAL EMERGENCIES. By Adolph G. DeSanctis, M.D., Professor of Pediatrics, Postgraduate Medical School, New York University-Bellevue Medical Center; and Charles Varga, M.D., Instructor in Pediatrics, Postgraduate Medical School, New York University-Bellevue Medical Center. 51 illustrations. The C. V. Mosby Company, St. Louis, 1951. 284 pages. $5.00.

This book had its beginning as a guide to the resident staff of the hospitals with which Dr. DeSanctis is associated and as a compendium for use in the pediatric courses of the Postgraduate Medical School. In these capacities it underwent several revisions, culminating in a privately printed edition.

The present volume is the outgrowth of this earlier material. It is therefore better organized and more complete than might be the case were it an initial effort of the authors.

There is a chapter each devoted to cardiovascular, gastrointestinal, genito-urinary, neurological, and respiratory emergencies. There is also a chapter each on drowning, poisoning, care of the premature infant, and miscellaneous emergencies.

The final chapter is an illustrated one on pediatric procedures. The book completely fulfills the purpose for which it was written and should be useful to pediatricians and others seeing infants and children in their practice.

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PRINCIPLES AND PRACTICE OF OBSTETRICS—10th Edition. By J. P. Greenhill, M.D., Attending Obstetrician and Gynecologist, the Michael Reese Hospital; Obstetrician and Gynecologist, Associate Staff, the Chicago Lying-In Hospital; Professor of Gynecology, Cook County Graduate School of Medicine. (Originally by Joseph B. DeLee.) 1,140 illustrations, 194 in color. W. B. Saunders Company, Philadelphia, 1951. 1,020 pages. $12.00.

In this tenth edition of DeLee's "Obstetrics" Greenhill appears for the first time as the sole author, although DeLee's name still is retained on the back of the cover, beneath that of Greenhill. On the title page it is noted that the text originally was written by Joseph B. DeLee but he is not otherwise identified except in the last line of the preface, where he is called "one of the greatest obstetricians of all time." When it is time for the next edition of this important work, the author and publishers might consider including a brief biographical sketch of DeLee, at least to the extent of a paragraph in the preface, because by then the book will be read by many with no first-hand knowledge of how obstetrics blossomed in the Chicago area early in the twentieth century under this master's leadership.

It is regrettable that Greenhill has permitted the size of the new edition to exceed that of its predecessor by some nine pages instead of making a drastic cut in total bulk. While it is true that many deletions have been made, the gaps have been more than filled by new material. The author states that he has "practically rewritten the entire book" and that "not a single page remains as it was." In a way this is true, but only in the sense that the material has been physically rearranged with respect to positioning on the various pages. Obviously the major portion of the text has not been changed because obstetrical practice is not appreciably different from what it was in 1947. A glance at the table of contents would suggest drastic changes in the new edition but one soon discovers that this results merely from the extirpation of fifty per cent of the "section" numbers and two of the chapter numbers. There has been a certain amount of amalgamation of old chapter headings, as well as the insertion of two new chapters, one by Helene Deutsch dealing with the psychology of pregnancy and one to accommodate vomiting of pregnancy, the discussion of which logically has been removed from the chapter on toxemias. The format of the table of contents has been improved greatly by better spacing and more attractive type, and throughout the book there are evidences of increased spacing between words so that the pages appear less crowded.

All of the recent advances in obstetric thinking and practice appear to have been included, and certainly this volume continues to merit its position as one of the most popular American reference works on obstetrics. There would seem to be little need to say more about a book which has been a best-seller for almost 40 years.

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THERAPY OF DERMATOLOGIC DISORDERS—Including a Guide to Diagnosis and a Dermatologic Pharmacopeia. By Samuel M. Peck, M.D., Dermatologist to the Mount Sinai Hospital; Associate Clinical Professor of Dermatology, Columbia University; and George Klein, M.D., Assistant Clinical Professor of Dermatology, New York Medical College. Lea and Febiger, Philadelphia, 1951. 383 pages. $6.50.

A unique approach to the treatment of skin disorders that is of great value to both the general physician and the dermatologist.

An unusual feature of the book, particularly helpful to the non-specialist, consists of topographical charts showing, by means of a code, the skin disorders most commonly seen in any given location. After referring to the code and the indicated diagnosis the reader will find a concise description of the disease and its treatment.

The dermatologist will be more interested in the last third of the book which is an excellent dermatologic pharmacopeia. Practically all of the drugs, both old and new, which are used in treating dermatologic disorders are discussed as to origin, action and use. Many valuable prescriptions are given.

A separate chapter by William Leifer briefly summarizes the diagnosis and treatment of venereal diseases.

This book is a valuable aid to anyone interested in the dermatoses.

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REVIEW OF PHYSIOLOGICAL CHEMISTRY. By Harold A. Harper, Ph.D., Professor of Biology, University of San Francisco, Lecturer in Surgery, University of California School of Medicine. Third Edition. University Medical Publishers, P.O. Box 761, Palo Alto. 260 pages. $3.50.

This small and economically published book fulfills the author's stated intentions in that it concisely presents fundamentals of physiological chemistry with attention to their application to medicine. Controversial topics and certain very recent advances have been avoided altogether or noted but briefly. The field is satisfactorily reviewed.

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Correction:

The price of "Atlas of Human Anatomy," Volumes I and II, by M. W. Woerdeman, published by the Blakiston Company, Philadelphia, is $5.50 per volume and $11 per set. In the notice accompanying the review published in the August issue of CALIFORNIA MEDICINE, the price was given incorrectly as $10 per volume, $18 per set.